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OF THE USSR

(ZHURNAL OBSHCHEI KHIMII)

IN ENGLISH TRANSLATION

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IVAN NIKOLAEVICH NAZAROV

I.V. Torgov

On July 30, 1957, Academician I.N. Nazarov died suddenly at the age of 51, while in Avignon (France) for professional reasons. Our nation lost one of its best sons and science lost a great organic chemist.

Ivan Nikolaevich was born on June 12, 1906 of a peasant family in Koshelev, Vladimir Province (now the Gorkii district). He belonged to the generation of Soviet scientists, members of the working intelligentsia, for whom the Great Socialist October Revolution opened up great opportunities in science. In 1922 he finished secondary school and became at first a teacher in his native town and then a school inspector for the district public schools in Murom. In 1927 he entered the Timiryazev Agricultural Academy and,on finishing his training there (1931), he became a student at the Leningrad State University, where he worked under the direction of one of the foremost Russian chemists – Academician A.E. Favorskii. In 1934 he moved to Moscow to work in the newly organized Institute of Organic Chemistry, where he continued to work for the rest of his life. For his work "Metallic ketyls of the aliphatic and aliphatic-aromatic series" he was awarded the degree of Candidate in Chemistry in 1935.

In 1936 Nazarov was the leader of a group investigating the synthesis of film-forming materials and started his outstanding work on the chemistry of acetylene and vinylacetylene. In 1941 he defended his PhD thesis on the theme: "Investigations in the field of acetylene derivatives. Synthesis of vinylacetylene alcohols and their reactions." From 1940 he directed the Vinylacetylene Laboratory, which was renamed in 1946 the Laboratory of Unsaturated Compounds and in 1954, the Laboratory of Fine Organic Synthesis.

When World War II began, Nazarov and the group he directed were among the first scientific workers to help in the war effort. The production and application of carbinol adhesive (a substance based on vinylacetylene polymers) was organized for cementing plastics, metals, glass, etc., and this was of great importance in machine construction and military servicing technology. In 1942 he. was awarded a Stalin prize for preparing and putting into use carbinol adhesive. Despite the intensive practical work he was carrying out and the difficult wartime conditions, he. continued his investigations on the reactions of acetylene and vinylacetylene derivatives. In 1946 Ivan Nikolaevich was awarded the Stalin Prize of the First Order for his work in this field and in the same year he was elected as a Corresponding Member of the Academy of Sciences, USSR. After the war his scientific activities developed to a great extent. He synthesized a series of physiologically active substances (anesthetics), materials related to steroids, heterocyclic compounds and, quite recently, natural terpenes and terpenoids. Work of great theoretical value was undertaken in the field of stereochemistry and diene synthesis.

In 1953 he was elected an Active Member of the Academy of Sciences, USSR. He kept his great enthusiasm for science to the end of his days. He was able to inspire his colleagues and especially youth with a great interest in it. He successfully coupled his productive scientific activity with teaching work as from 1948 he was head of the organic chemistry department of the Lomonosov Institute of Fine Chemical Technology of Moscow. In heading the large scientific groups of the Institute of Organic Chemistry and of the Institute of Fine Chemical Technology, he built up a large school of synthetic chemists. More than forty scientists defended their candidate and doctorate theses under his direction. Numerous students and followers of Nazarov continue to develop his ideas in the Academies of Science of the republics and in a number of branches of the Academy of Sciences, USSR.

The name of I.N. Nazarov is not only known widely in our country, but also beyond its borders. He was elected a member (in 1955) of the German Academy of Naturalists in Halle and, in 1956, Corresponding Member of the Berlin Academy of Sciences. The government of the USSR has valued his work highly and awarded him

IVAN NIKOLAEVICH NAZAROV

1906 - 1957

the Order of the Red Banner of Labor twice (in 1944 and 1953), the Order of the Red Star (in 1945) and medals. He was a model man and citizen, whose highest aim was to serve science and the people.

It is hard to give a summary of I.N. Nazarov's works as their number approaches 500 and therefore we must limit ourselves to illustrating the main directions of his scientific activity only.

Investigations in the Field of Branched Ketones

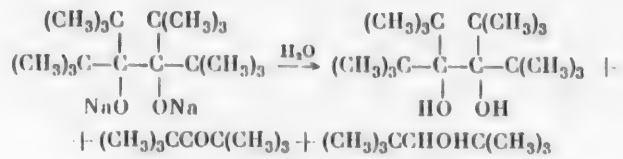
Nazarov made his first investigations in 1931-1935 in the laboratory of Academician A.E. Favorskii, and these were devoted to the conversions of free radicals of the aliphatic-aromatic series, the so-called metallic ketyls. The latter were formed by treating ketones of the type $(CH_3)_3CCOR$ and C_6H_5COR with alkali metals (mainly sodium). The intensely colored metallic ketyls are dimerized more or less readily into pinacone alcoholates.

$$(CH_3)_3CCOR \xrightarrow{Na} (CH_3)_3CCRONa \rightarrow (CH_3)_3CC(R,R)-C(R,R)C(CH_3)_3 \quad (NaO,\ ONa)$$

$$C_6H_5COR \xrightarrow{Na} C_6H_5C(R)(ONa) \rightarrow C_6H_5-C(R,R)-C(R,R)-C_6H_5 \quad (NaO,\ ONa)$$

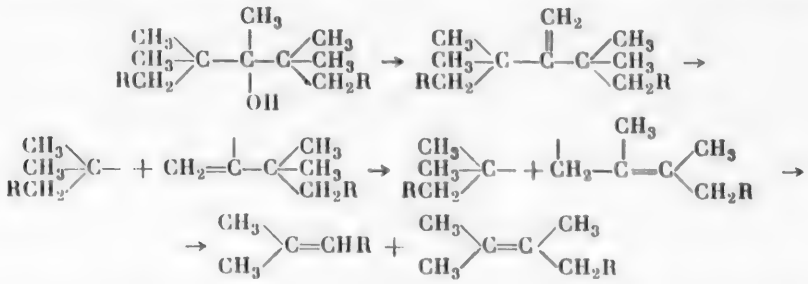
When R is a primary or a secondary alkyl radical, the ketyl is unstable, but as the molecular weight and branching of the radical increase, the metallic ketyls become more stable and an equilibrium is established be-

tween them and the pinacone alcoholates. Thus, sodium ketyls from the ketones $(CH_3)_3CCOC(C_2H_5)_2CH_3$ and $(CH_3)_3CCOC(C_2H_5)_3$ are not dimerized after many months, while sodium ketyls from the ketones $C_6H_5COC(C_2H_5)_2CH_3$, $C_6H_5COC(CH_3)_3$ and $C_6H_5COC(C_2H_5)_3$ may be isolated in the crystalline state. When treated with water, pinacone alcoholates decompose to give only some pinacone, but mainly the starting ketone and the corresponding alcohol, for example:



This investigation in the field of metallic ketyls was the subject of Nazarov's Candidate Thesis [1].

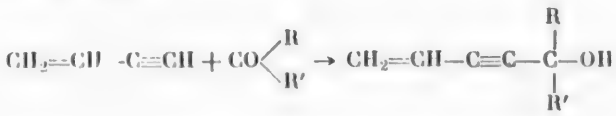
By treating branched aliphatic ketones with methylmagnesium bromide, he. prepared a series of tertiary alcohols and investigated their dehydration. Distillation of these alcohols with small amounts of iodine gave 1,1-dialkylethylenes; while if the reaction was carried out in the presence of sulfonic acids, the molecules were cleaved. The same type of cleavage occurred when these ethylene hydrocarbons were heated with sulfonic acids, with the break occurring at the bond connecting the tertiary radical to the ethylene residue to form two lower olefins. In the case of identical alkyl substituents, the process may be illustrated by the following scheme:



The tert -alkyl radical formed during the decomposition eliminates hydrogen and is converted to a dimethylalkylethylene, while the tert -alkylvinyl radical adds hydrogen to form a tetra-substituted ethylene [2].

Investigations in the Field of Vinylethynylcarbinols

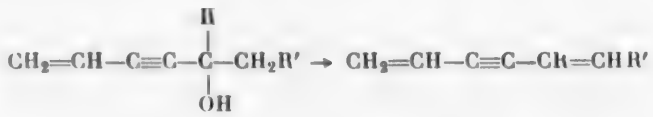
In 1936 he began a systematic investigation in the field of vinylacetylene. He showed that when condensed with ketones by A.E. Favorskii's method, vinylacetylene readily formed vinylethynylcarbinols in the presence of powdered potassium hydroxide [3]. The reaction proceeds more smoothly than with acetylene itself and the carbinol yields are often over 90%.



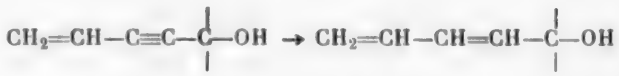
Vinylacetylene alcohols were found to be very interesting compounds, which undergo particularly numerous and varied conversions; they opened up a new and fascinating field in organic chemistry. Readily polymerized and passing through stages of sirups of various viscosities, they finally form a solid, glassy mass. This made it possible to use the simplest dimethylvinylethynylcarbinol as an adhesive, capable of firmly cementing metals, glass, marble, porcelain, minerals and plastics. The product of partial polymerization of dimethylvinylethynylcarbinol, known as "Carbinol Cement," "Balsamin" and "Nazarov's Cement," has been applied widely in various branches of industry, optical, instrumental, electrotechnical, aviation, etc. [4].

The chemical behavior of vinylethynylcarbinols is very varied and is determined by the presence of a conjugated system of double and triple bonds and an extremely labile hydroxyl group. The reactivity of the hydroxyl groups of vinylethynylcarbinols is similar to that of triphenylcarbinol. They are readily esterified with organic

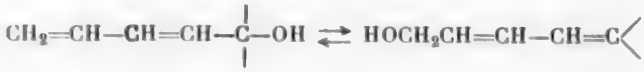
acids (in the presence of sulfuric acid) but the dehydration or normal tertiary alcohols does not occur here. When treated with hydrogen chloride, they exchange the hydroxyl for a chlorine even in the cold and when treated with alcohols (in the presence of sulfuric acid), they readily form ethers [5]. Tertiary vinylacetylene alcohols are dehydrated with 50% sulfuric acid at 50-60° to form divinylacetylene hydrocarbons and the yields are close to 90% in most cases.



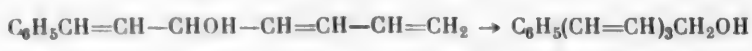
Other reactions of vinylethynylcarbinols are characterized by the presence of double and triple bonds. A selective method was found for reducing the triple bond to a double one, using a zinc-copper couple, and this gave diene alcohols [6].

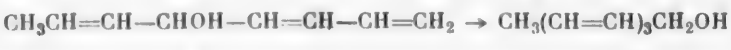


Dimethylbutadienylcarbinol and a series of secondary diene alcohols were prepared by this method. Diene alcohols readily undergo reversible anionotropic rearrangement.



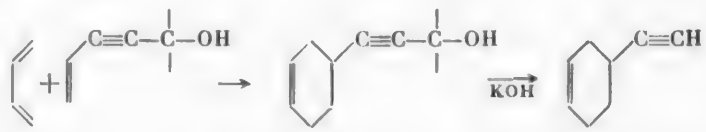
This rearrangement was then extended to cover polyene alcohols, which were prepared by reduction of secondary vinylethynylcarbinols with unsaturated substituents.



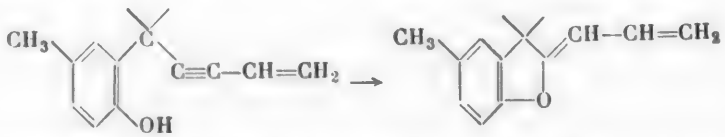


In these cases it was shown that the equilibrium was everywhere strongly displaced toward the formation of tertiary alcohols while the opposite is the case for halogen derivatives, ethers and esters, i.e., primary compounds are mainly formed.

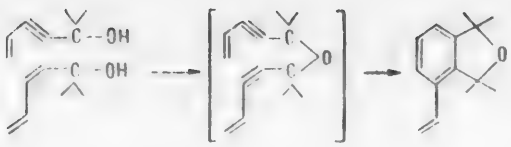
An example of a reaction in which only one vinyl group of vinylethynylcarbinol participates is that of diene synthesis which forms Δ^3-cyclohexenylethynylcarbinols [7].



In the presence of phosphoric acid, vinylethynylcarbinols are condensed with phenols in the same way as aliphatic alcohols, forming para-substituted phenols with a vinylacetylene side chain. However, if the para-position is occupied, the vinylacetylene radical occupies the ortho-position and the corresponding vinylacetylene phenols are cyclized at the moment of formation to allylidenecoumaranes, which were previously unknown [8].



An interesting reaction was discovered when vinylethynylcarbinols were heated with acidic reagents, in particular, ferric chloride [9]. This reaction gave a 50-70% yield (for the lower types) of vinylisocoumaranes, which polymerize similarly to styrene.



Investigation in the Field of Divinyl Ketones

One of the most interesting reactions of vinylethynylcarbinols is their isomerization to divinyl ketones [10], which occurs under the action of mercury salts by the following scheme:

$$CH_2{=}CH{-}C{\equiv}C{-}\underset{|}{\overset{|}{C}}{-}OH \rightarrow \left[CH_2{=}CH{-}\underset{|}{\overset{OH}{C}}{=}C{=}C\right] \rightarrow CH_2{=}CH{-}CO{-}CH{=}C$$

This reaction may be applied very widely; it occurs with tertiary, secondary and primary vinylethynylcarbinols. It proceeds particularly smoothly in alcohol solutions, giving up to 80% yields of the corresponding β-alkoxy ketones, which readily eliminate alcohol (when distilled with p-toluenesulfonic acid) to form divinyl ketones.

$$CH_2{=}CH{-}C{\equiv}C{-}\underset{|}{\overset{|}{C}}{-}OH \rightarrow CH_2{=}CH{-}CO{-}CH{=}C \underset{C_7H_7SO_3H}{\overset{ROH}{\rightleftharpoons}} ROCH_2CH_2COCH \parallel C$$

The reaction described is thus a simple method of preparing divinyl ketones with an unsubstituted vinyl group, which were completely inaccessible previously.

Also in 1938, a second method was discovered for preparing divinyl ketones with various substituents at the double bonds. This method was based on the hydration of divinylacetylene hydrocarbons in an aqueous methanol solution in the presence of mercury salts [11].

$$\text{>}C{=}\underset{|}{\overset{|}{C}}{-}C{\equiv}C{-}\underset{|}{\overset{|}{C}}{=}CH \xrightarrow{H_2O} \left[\text{>}C{-}\underset{|}{\overset{|}{C}}{-}COCH_2\underset{|}{\overset{|}{C}}{=}CH\right] \rightarrow \text{>}C{=}\underset{|}{\overset{|}{C}}{-}CO{-}CH{=}\underset{|}{\overset{|}{C}}{-}CH_2$$

It should be noted that attempts by other chemists to carry out such a hydration were unsuccessful. Hydration of dienynes proceeds through the intermediate formation of vinyl allyl ketones, which are irreversibly isomerized to divinyl ketones under the reaction conditions [12]. For a long time this type of divinyl ketone was assigned the structure of vinyl allyl ketone.

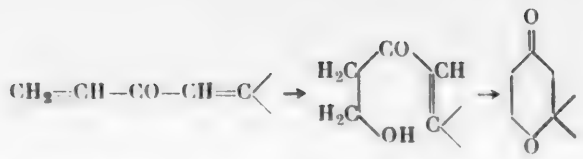
Recently a third method of preparing divinyl ketones was developed, based on the capacity of vinylacetylene and its homologs to undergo the Mannich reaction.

$$RCH{=}CR'C{\equiv}CH \underset{HN\text{<}}{\overset{CH_2O}{\longrightarrow}} RCH{=}CR'C{\equiv}CCH_2N\text{<} \xrightarrow{H_2O}$$

$$\rightarrow RCH{=}CR'COCH_2CH_2N\text{<} \rightarrow RCH{=}CR'COCH{=}CH_2$$

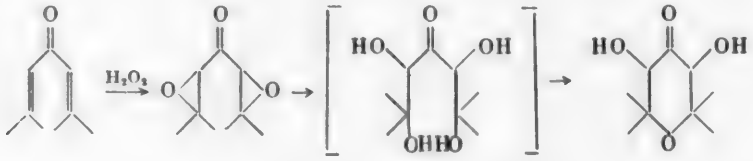
The vinylacetyleneamines thus formed may be hydrated to unsaturated amino ketones, which readily eliminate a secondary amine and give divinyl ketones with one free vinyl group while, at the same time, the other vinyl group may have various substituents [13].

Divinyl ketones are capable of various addition reactions which, in the case of unsymmetrically substituted divinyl ketones, have a sharply expressed stepped character. The activity of the double bond in addition reactions falls sharply when substituents are introduced at the vinyl groups and, simultaneously, the capacity of the divinyl ketones to polymerize also decreases [14]. Thus, water adds to unsymmetrically substituted divinyl ketones to form unstable unsaturated β-hydroxy ketones, which are cyclized under the action of acid to tetrahydro-γ-pyrones and, in an alkaline medium, readily eliminate water and revert to the starting divinyl ketones.

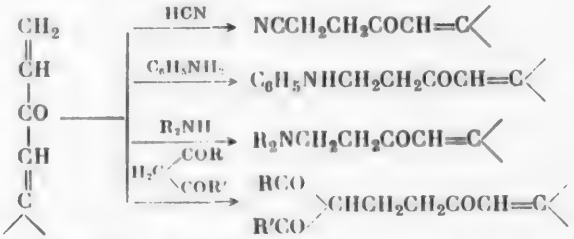


Alcohols add extremely rapidly to divinyl ketones, especially in the presence of acid catalysts, with the primary adding most readily, the secondary less readily and the tertiary alcohols with the most difficulty.

An interesting reaction is the oxidation of divinyl ketones in the presence of alkaline hydrogen peroxide. This gives keto dioxides which are hydrolyzed by solution in water to form intermediate ketotetrols which then undergo intramolecular cyclization to form 3,5-dihydroxytetrahydro-4-pyrones.

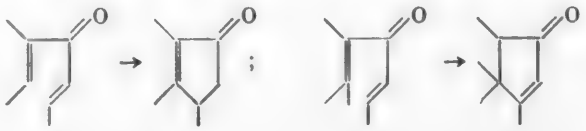


Secondary aliphatic amines, primary aromatic amines, hydrogen cyanide and compounds with an active hydrogen atom of the malonic and acetoacetic ester type add to divinyl ketones only at the unsubstituted vinyl group to give high yields of the corresponding derivatives [14].

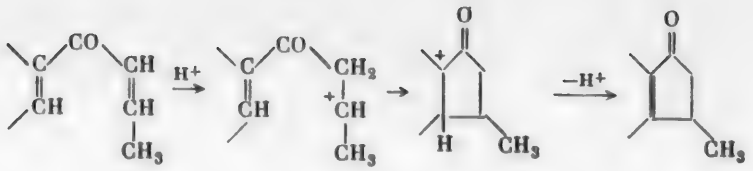


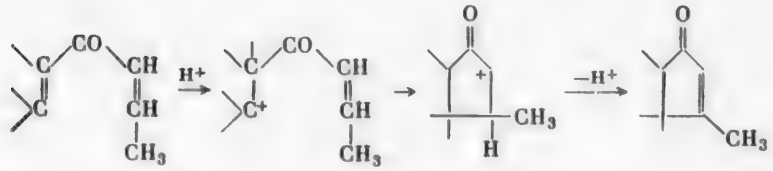
Hydrogen chloride and sulfide add to β-substituted divinyl ketones in the reverse order, i.e., first at the substituted vinyl group to form unstable tertiary β-chloro ketones and β-mercapto ketones [14].

A particularly interesting reaction of divinyl ketones, discovered in 1944, was the cyclization of these compounds to cyclopentenones [15], which occurs under the action of acids (phosphoric, formic, etc.).

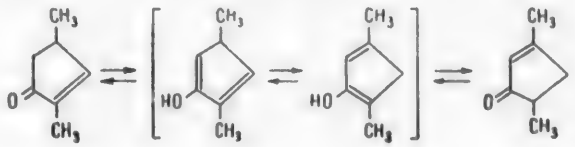


Divinyl ketones with an unsubstituted vinyl group do not undergo this reaction, but form the tetrahydro-γ-pyrones mentioned above. A thorough study of the cyclization with labeled atoms (deuterium) showed that it proceeded by an ionic mechanism and involved the free β-hydrogen of the vinyl group [16].

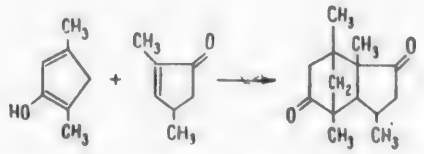




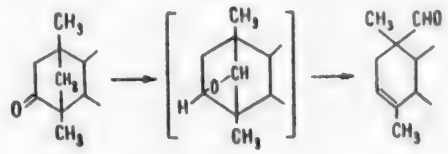
A study of the properties of the simplest 2,4-dimethyl-Δ^2-cyclopentanone led to the discovery of an interesting isomerization of the latter with migration of the double bond, proceeding by an enol mechanism under the action of acid and alkaline agents and also by heating [17].

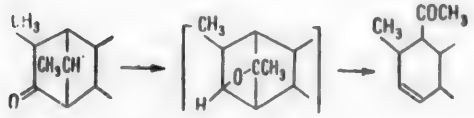


In the presence of alkaline agents, the dimethylcyclopentanones described above undergo an intermolecular diene condensation, forming complex polycyclic ketones with an endomethylene bridge and an angular methyl group.

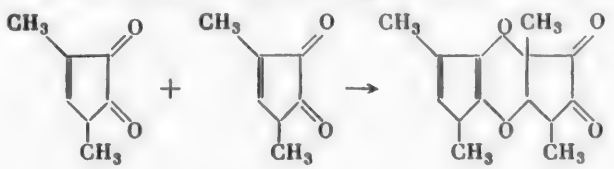


Under the action of hydrochloric acid, these cyclic ketones rearrange into aldehydes (or ketones) with transfer of the endomethylene group and the carbonyl oxygen into the side chain.





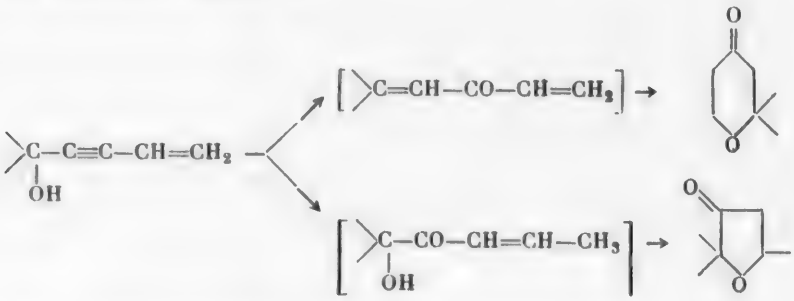
An interesting fact is the dimerization of 1,3-dimethyl-Δ^1-cyclopentendione-4,5 (obtained from 2,4-dimethyl-Δ^2-cyclopentenone by oxidation with SeO_2), which proceeds in the cold in the presence of alkaline agents. This condensation proceeds by a type of diene synthesis, giving a dioxane derivative.



Thus, on the basis of cyclopentenones, and ultimately acetylene, it was found possible to synthesize polycyclic compounds of the camphene type by a simple method.

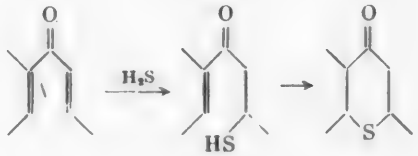
Investigations in the Field of Heterocyclic Compounds

In investigating vinylethynylcarbinols it was established that when they were hydrated under the conditions of a Kucherov reaction (aqueous solution of mercuric sulfate) they were cyclized to tetrahydro-γ-pyrones. It was later found that the reaction proceeded in two directions: to form pyrones (through intermediate divinyl ketones) and furanones (through unsaturated α-ketols) [18].

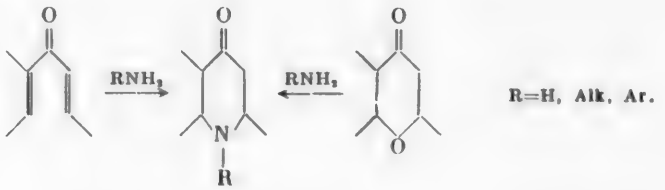


In the case of isopropylvinylethynylcarbinol the second direction predominates.

With the discovery of practicable methods of preparing divinyl ketones, it became possible to synthesize other six-membered heterocycles on the basis of the ketones. Thus, it was shown that β-mercapto ketones (prepared by treating divinyl ketones with hydrogen sulfide, see above) were readily cyclized under the effect of sodium acetate to tetrahydrothiopyrones [14].

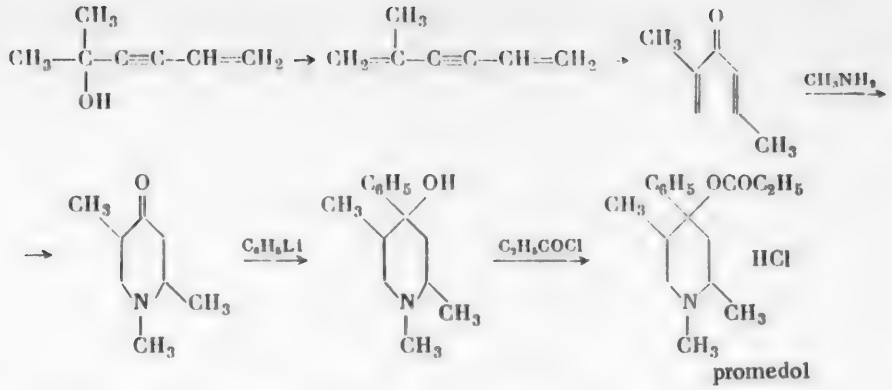


Treatment of divinyl ketones with ammonia and primary amines gave various piperidones (often in yields of more than 80%). Instead of divinyl ketones, one may start with the corresponding methoxy ketones or tetrahydro-γ-pyrones [19].



The reaction between divinyl ketones with a free vinyl group and ammonia proceeds with the greatest difficulty to give only small yields of the corresponding piperidones as derivatives.

The conversion of divinyl ketones to heterocyclic compounds was an outstanding accomplishment and it made possible the synthesis of physiologically active materials. Thus, starting with γ-piperidones, 4-phenylpiperidols were prepared, whose ethers have an exceptionally high anesthetic activity. The hydrochloride of 1,2,5-trimethylpiperidol-4 propionate is now widely used in medicine, under the name of "promedol," as a substitute for morphine and, since 1953, has been produced on an industrial scale by the following scheme [20]:

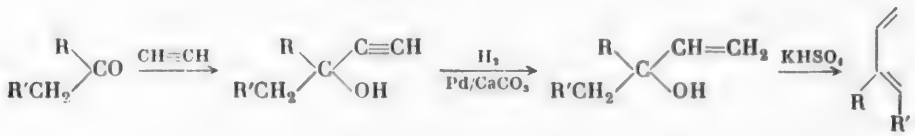


In contrast to morphine, promedol does not have a habit-forming effect (morphism) on patients and is therefore safer for clinical use and its effect is greater by a factor of 2-3 than that of morphine. The promedol stereoisomer, isopromedol, which is obtained as a side product, is more active than morphine by a factor of 4-5.

Using this method, various γ-piperidols with aliphatic, alicyclic and aromatic substituents in the piperidine ring, as well as piperidines with condensed cyclic systems were synthesized.

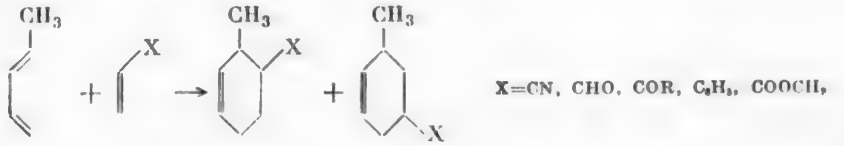
Investigations in the Field of Acetylene and Diene Syntheses

I.N. carried out extensive investigations in the field of diene synthesis. First of all, we should mention the methods he developed for the preparation of various dienes, starting from acetylene alcohols, by the scheme:

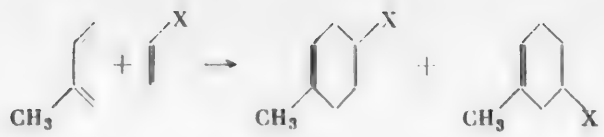


The acetylene alcohols needed for this synthesis were first prepared by Favorskii's method by treating ketones with acetylene in the presence of powdered potassium hydroxide. Aldehydes and aliphatic-aromatic and aromatic ketones did not undergo this reaction. However, it was found that on carrying out the reaction under pressure the rate of the process increased to such an extent that it was possible to condense with acetylene aldehydes and ketones of the most varied structure, including such alkali-sensitive aldehydes as acetaldehyde and inert ketones of the acetophenone and benzophenone types [21]. The acetylene alcohol yields were increased considerably by the addition of small amounts of ethanol or butanol. Acetaldehyde gave 43% of the corresponding alcohol, propanol, 45% and cyclohexanone and acetone, over 90%. The development of a simple method for the preparation of acetylene alcohols allowed a new approach to the synthesis of a series of important dienes, including isoprene, which are required for the preparation of rubbers.

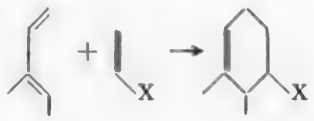
These investigations were closely connected to other fields being developed by I.N., such as his work on the synthesis of isoprenoids and steroid compounds. They also gave an impetus to theoretical investigations in the field of the stereochemistry and laws of diene synthesis. The structural direction of the reaction of 1-substituted butadienes with unsymmetrical dienophiles was studied on the example of piperylene. Here a mixture of adducts was always formed and this contained 85-90% of ortho-isomers and 5-15% of meta-isomers [22].



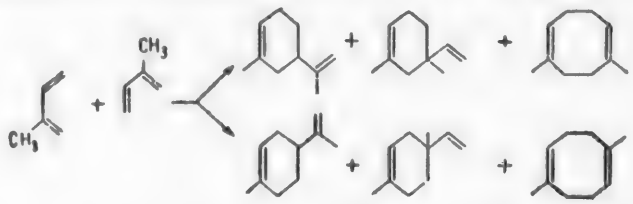
In the condensation of isoprene and other 2-substituted dienes with unsymmetrical dienophiles, a mixture of adducts was also formed and this contained 80-90% of para-isomers and 10-20% of meta-isomers.



With an increase in the volume of the substituents both in the diene and in the dienophile, the percent of the meta-isomer fell and, for example, in the condensation of 2-tert-butylbutadiene with α-isopropylacrylic acid, the para-isomer was obtained exclusively. The condensation of 1,2-substituted dienes with unsymmetrical dienophiles had an almost unidirectional character and, in most cases, led to the formation of only ortho-isomers.

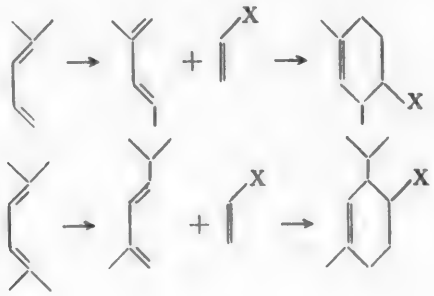


Interesting results were obtained in the dimerization of isoprene. It was found that at low temperatures (100°), despite the usual structural direction, isoprene dimerized with the formation of mainly the meta-isomer (diprene, 60-65%), while at 200-250° the dimerization proceeded by the normal scheme and, in this case, the main dimer was the para-isomer (dipentene, 70-75%). In addition to all the four possible six-membered dimers, 3-5% of two isomeric dimethylcyclooctadienes were also isolated in the dimerization of isoprene [23].



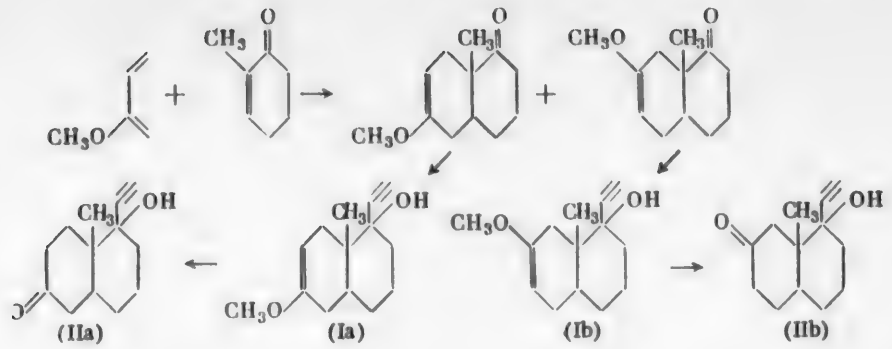
Despite the fact that many chemists were occupied with investigating the dimerization of isoprene for several decades, this involved problem was only finally solved after the work of I.N. Nazarov; in parallel, a study was also made of the dimerization of trans-piperylene and it was shown that, in this case, the direction of the reaction did not depend on temperature and led to the formation of all the theoretically possible dimers with strong predominance of the ortho-isomer.

Diene condensation involving gem-substituted dienes proceeded peculiarly. 1,1-Dimethylbutadiene and 1,1,4,4-tetramethylbutadiene underwent diene synthesis only after preliminary isomerization into the 1,3-disubstituted dienes.

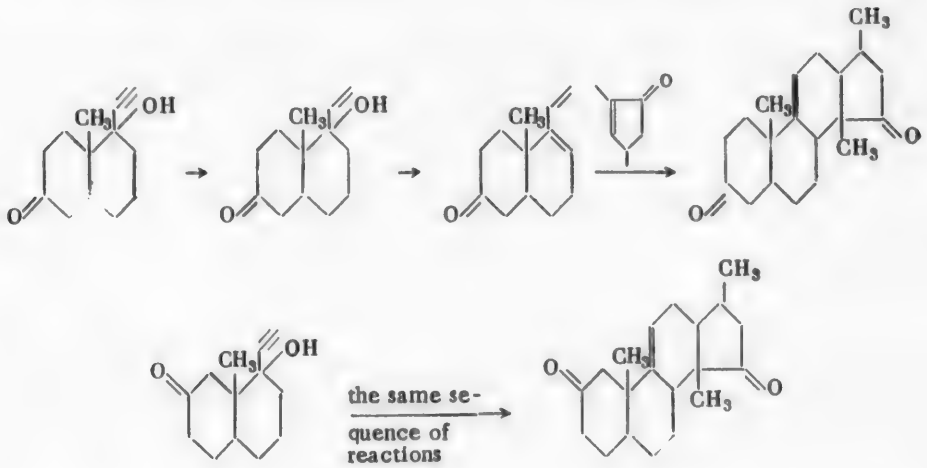


Investigations on the Synthesis of Steroid Compounds

The first works on the synthesis of steroid compounds were undertaken on the basis of a diene synthesis. Thus, the condensation of 2-methoxybutadiene with methylcyclohexenone yielded a mixture of methoxyoctalones, which condensed with acetylene to give a mixture of acetylene alcohols (Ia) and (Ib).

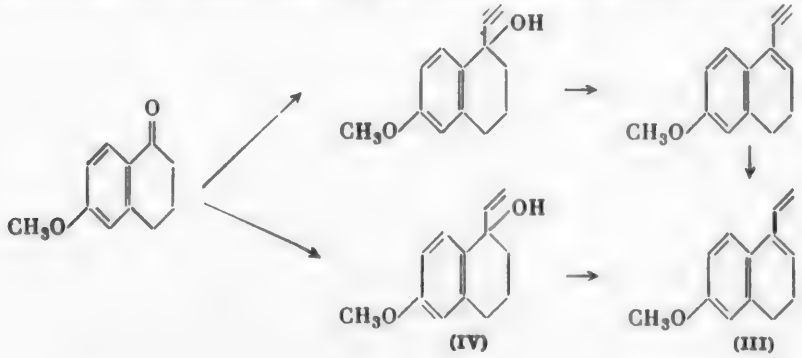


Acid hydrolysis of these alcohols gave acetylene alcohols (IIa) and (IIb), which were readily separated by crystallization. Selective hydrogenation of the latter into vinylcarbinols and subsequent dehydration led to bicyclic ketodienes, 1-vinyl-9-methyl-Δ^1-octalone-6 and 1-vinyl-9-methyl-Δ^1-octalone-7, the first of which condensed with 2,4-dimethyl-Δ^2-cyclopentenone-1 to give a mixture of stereoisomeric tetracyclic steroid diketones [24].

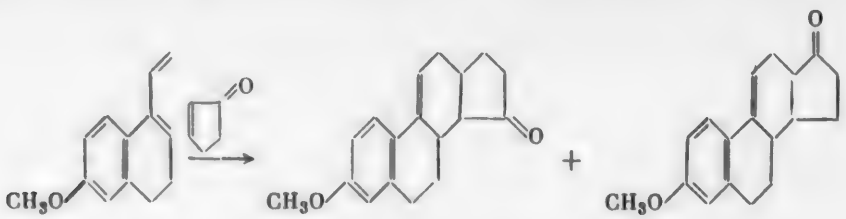


Determination of the structures of the latter showed [25] that all the stereoisomers had a keto group in position 15 and differed from each other only in the steric disposition of the hydrogen atom at C_8 and the substituents (H and CH_3) at C_{13}–C_{14}.

By this method it was possible to obtain not only isomers of androstane derivatives, but also of estrane [26]. The 1-vinyl-6-methoxy-3,4-dihydronaphthalene (III) required for this was obtained by two methods. In the first method, 6-methoxytetralone was condensed with acetylenemagnesium bromide (obtained at −70° from ethylmagnesium bromide and acetylene) under pressure into an acetylene alcohol, which was converted into the diene by dehydration and subsequent hydrogenation. The second method consisted of the action of vinylmagnesium bromide on methoxytetralone; the vinylcarbinol (IV) thus formed gave diene (III) on dehydration.

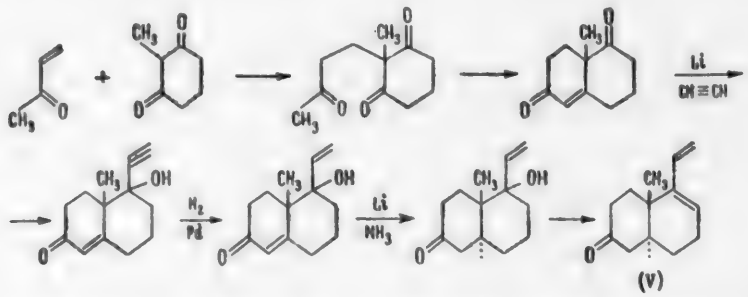


Condensation of the diene with cyclopentenone yielded two steroid ketones with keto groups in positions 15 and 17.

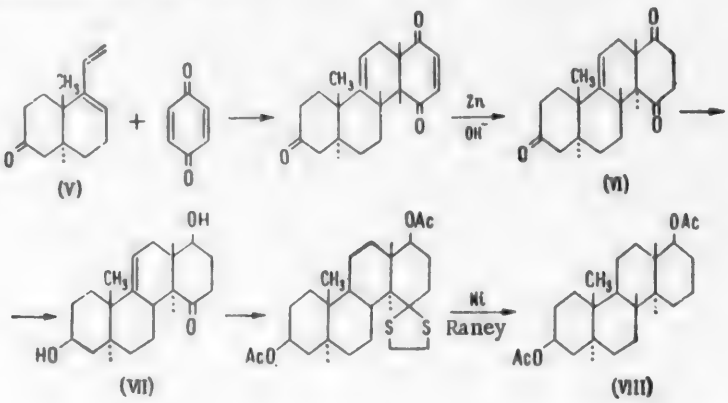


Cyclic unsaturated sulfones (see section on heterocycles) were also used as the dienophile and this gave steroid compounds with a sulfur hetero atom in ring D.

The diene condensation naturally yielded compounds with cis-coupling of rings A and B and C and D. For the preparation of steroid compounds with trans-coupling of the rings, another method was found and this combined the diene synthesis with the Michael condensation [27].

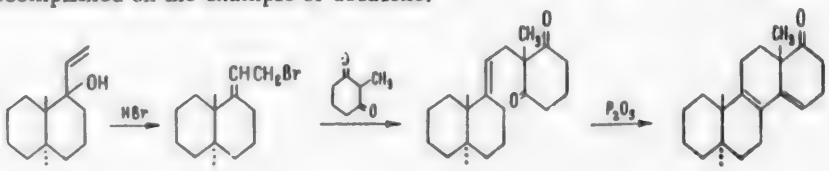


Condensation of dienone (V) with quinone, with subsequent reduction and isomerization on alkaline aluminum oxide, yielded triketone (VI). To remove the keto group in position 15, this triketone was hydrogenated with Raney-Ni to ketodiol (VII). The series of reactions presented in the scheme below yielded the diacetate of D-homo-18-nor-Δ^{8}-androstenediol-3,17a (VIII).

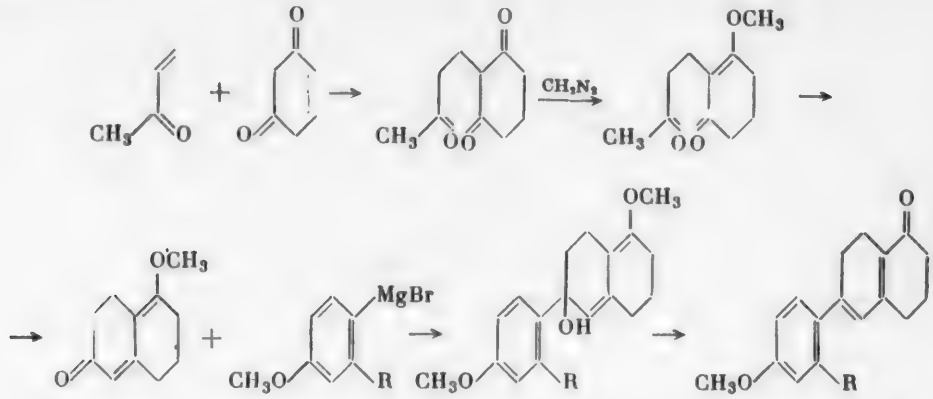


Compounds (VII) and (VIII) showed an activity close to the activity of androsterone [28].

To prepare compounds with a keto group in position 17, as in natural steroids, the following chain of reactions was also accomplished on the example of decalone:

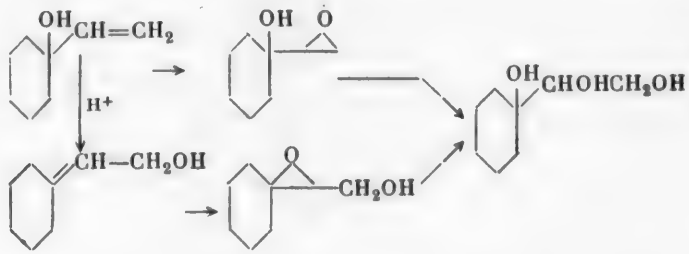


On the basis of dihydroresorcinol, various analogs of steroid compounds were also synthesized, for example, analogs with ring B open [29].



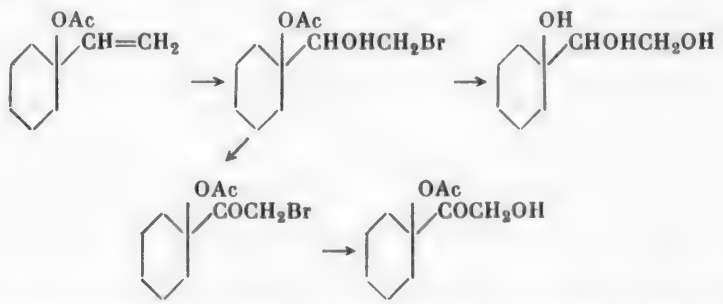
Since, of the natural steroids, there is especial interest in the adrenocortical hormones with a hydroxyacetone or a dihydroxyacetone grouping in position 17, work was undertaken on a search for simple and convenient methods of introducing these groups.

For the preparation of a glycerol chain, the so-called glycide method was developed and this consists of oxidizing allyl alcohols with hydroperoxides and subsequent hydrolysis (or acidolysis) of the epoxy alcohols formed [30].

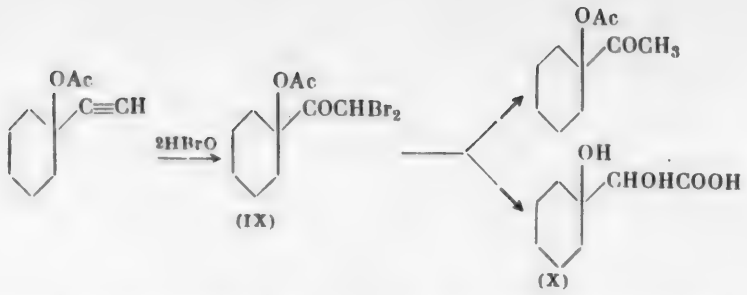


With an asymmetric carbon atom in the ring, oxidation of the primary and tertiary allyl alcohols must lead to compounds of different steric configurations, which is important for physiological activity.

For the preparation of a glycerol or a dihydroxyacetone chain, the bromohydrin method was found to be convenient and this consists of oxidizing tertiary acetylene alcohols with N-bromoacetamide or hypobromous acid. In the case of acetates of the alcohols, the bromohydrins obtained were readily hydrolyzed into the glycerol derivatives referred to above. By oxidation, the bromohydrins could be converted into a bromo ketone and hydrolysis of the latter gave a compound containing a dihydroxyacetone chain.



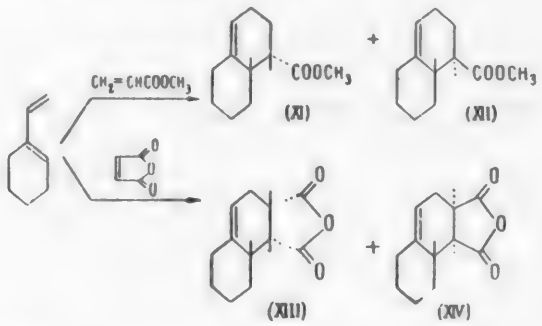
The addition of two molecules of hypobromous acid to the acetate of the acetylene alcohol quantitatively formed the dibromo ketone (IX), which was debrominated to give the acetate of 1-acetylcyclohexanol-1. Hydrolysis of the dibromo ketone led to isomerization into a glyceric acid derivative (X).



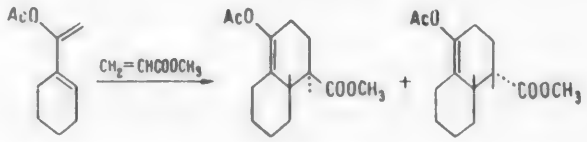
Similar conversions were accomplished also with ortho-substituted cyclohexanones, o-methylcyclohexanone and cis- and trans-α-decalones, whereby the configurations of all the compounds were strictly proved.

Investigations in the Field of the Stereochemistry of Carbocyclic and Heterocyclic Compounds

I.N. Nazarov attached extremely great importance to the study of stereochemistry, especially in the field of natural compounds and, in particular, of steroids, due to which broad investigations of the stereochemistry of cyclic compounds were undertaken. With this aim, a detailed study was made of the steric direction of some diene condensations, with the help of which, the synthesis of stereoisomers of cyclic mono- and dicarboxylic acids was accomplished. Thus, it was found that the condensation of 1-vinyl-Δ^1-cyclohexene with acrylic ester at 50° gave the syn-isomer (XI) as the main reaction product, while at 170° a mixture of isomers was formed from which was isolated 25% of the syn-isomer (XI) and 32% of the anti-isomer (XII). The condensation of vinylcyclohexene with maleic anhydride proceeded with a similar selectivity and at 0° yielded a mixture of the syn-cis-adduct (XIII) and the anti-cis-adduct (XIV) in a ratio of 10:1 [31].

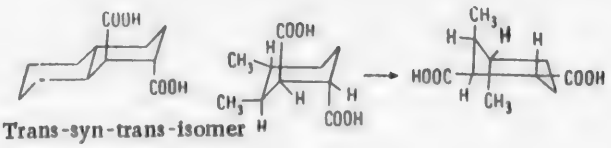


With maleic anhydride, trans-1,2-dimethylbutadiene gave only the endo-adduct. The reaction with 1-α-acetoxyvinylcyclohexene had a different character and proceeded, even under mild conditions, contrary to the rule of the maximum accumulation of unsaturation. Thus, in the condensation of this diene with acrylic ester, even at low temperature the anti-adduct was formed predominantly and the relative amount of it fell with an increase in temperature, while the percent of the syn-adduct increased simultaneously [32]. Condensation of acetoxyvinylcyclohexene with maleic anhydride at 0° led predominantly to the anti-cis-adduct.



A detailed study of the interconversions of adducts (XIII) and (XIV) (isomerization of the half esters and diesters with sodium methylate, thermal isomerization, hydrogenation and hydrogenolysis of the ketolactonoacids) made it possible to synthesize seven stereoisomers of decalin-1,2-dicarboxylic acid (of the eight possible) and prove their configurations and conformations. The eighth isomer (trans-syn-trans-) must be unstable since it can only exist (in the case of the chair form of the ring) with a diaxial disposition of the carboxyl groups, i.e., an

energetically disadvantageous structure. Its anhydride must possess a bed-form structure. The fact that this isomer, whose existence is energetically improbable, was not obtained confirms the accuracy of the configurations assigned to the other seven isomers.



Trans-syn-trans-isomer

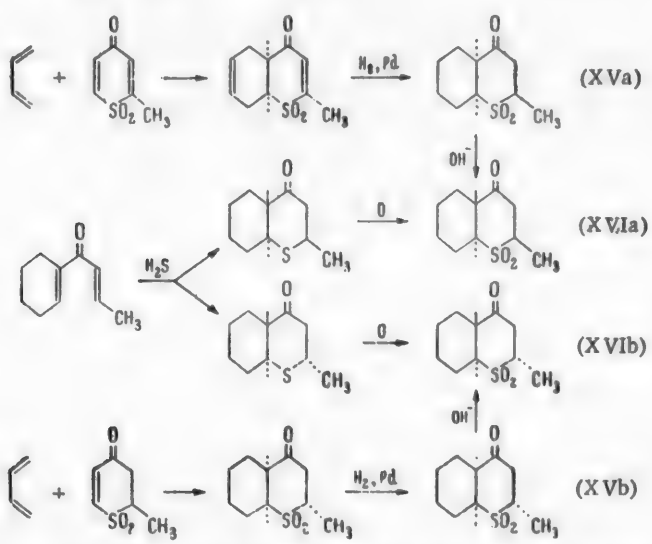
A similar investigation was also made on the adducts of 1,2-dimethylbutadiene with maleic anhydride. In this case, the cyclohexane ring was capable (in contrast to the rigid decalin system) of ready conversion by which an axial group was converted into an equatorial one and thus (see scheme) the preparation of the trans-cis-trans-isomer (analogous to the trans-syn-trans-compound presented above) became possible. Actually, all eight of the theoretically possible isomers of 3,4-dimethylcyclohexane-1,2-dicarboxylic acid were synthesized [33].

An interesting rule was observed in the oxidation of the stereoisomeric adducts with peracetic acid and osmium tetroxide. For example, the oxidation of syn- and anti-Δ^4-octalin-1-carboxylic acids proceeded similarly to hydrogenation, i.e., from the opposite direction to the shielding carboxyl group. On the other hand, the oxidation of syn-cis-Δ^4-octalin-1,2-dicarboxylic acid did not proceed selectively and led to a mixture of α- and β-oxides.

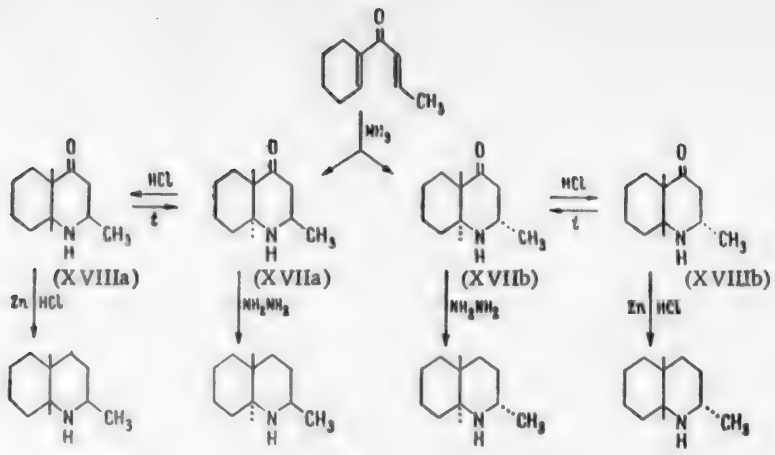
Stereochemical investigations were also carried out on heterocyclic compounds. Thus, all four theoretically possible racemates of the dioxides of 2-methylhexahydro-1-thiochromanone-4 were obtained by the scheme presented below.

Under the action of sodium methoxide, the cis-sulfones (XVa) and (XVb) were readily isomerized into the trans-isomers (XVIa) and (XVIb) [34].

Interesting conversions were accomplished on the example of 2-methyldecahydroquinolones-4. The action of ammonia on propenyl-Δ^1-cyclohexenyl ketone formed two stable isomeric trans-decahydroquinolones (XVIIa) and (XVIIb). Treatment of them with hydrogen chloride yielded the hydrochlorides of the isomeric cis-decahydroquinolones (XVIIIa) and (XVIIIb), which were extremely unstable as the free bases and changed into the stable trans-isomers (XVIIa and b) during storage or on heating.

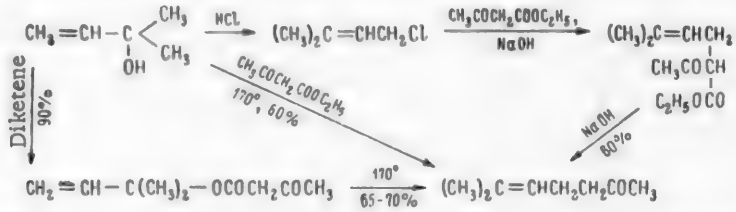


Reduction of the alkali-stable trans-isomers (XVIIa and b) by the Kizhner method and reduction of the acid-stable cis-isomers (XVIIIa and b) by the Clemmensen method gave all four possible stereoisomers of 2-methyldecahydroquinoline.

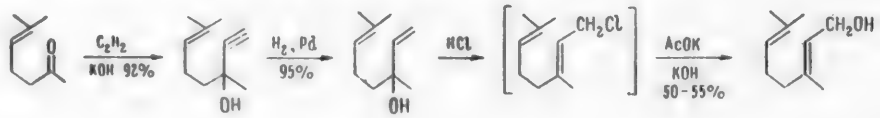


Investigation in the Field of Isoprenoids

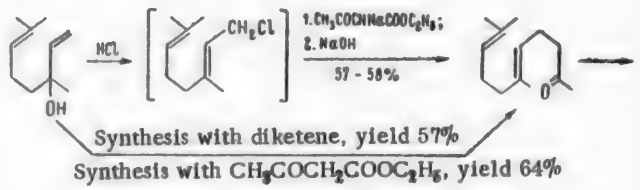
The successful condensation of aldehydes and ketones with acetylene under pressure (see above) made various vinylcarbinols and dienes accessible and opened up a method of synthesizing isoprenoids, which I.N. began to develop in 1954. Treatment of dimethylvinylcarbinol with hydrogen chloride or bromide gave the primary halides and treatment of these with acetoacetic ester in the presence of sodium hydroxide (with subsequent hydrolysis and decarboxylation) yielded methylheptenone, the main starting material for the synthesis of isoprenoids. Methylheptenone was also prepared by two other methods; condensation of dimethylvinylcarbinol with acetoacetic ester (yield 60-65%) and pyrolysis of the acetoacetate of dimethylvinylcarbinol (yield 65-70%).

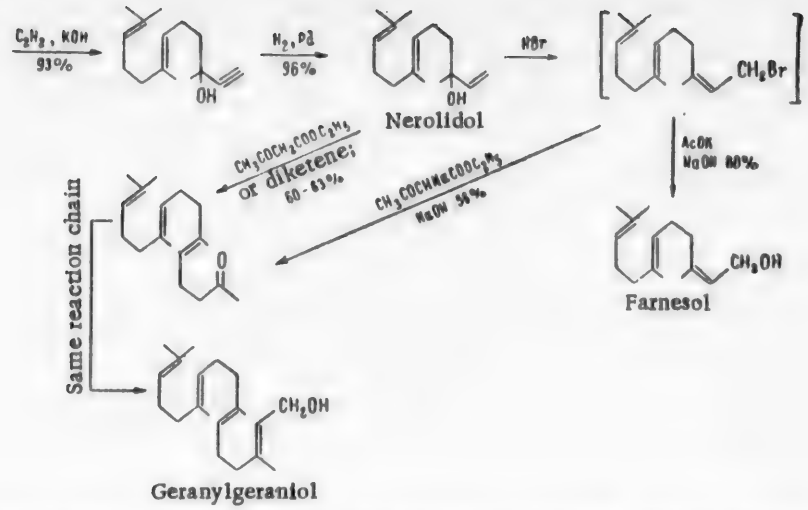


Ethynylation of methylheptenone led to dehydrolinalool, which gave a high yield of pure linalool on selective hydrogenation [35]. Its isomerization into a mixture of geraniol and nerol was also accomplished; here the yield was 50-55%, while not more than 30% could be obtained up to that time.



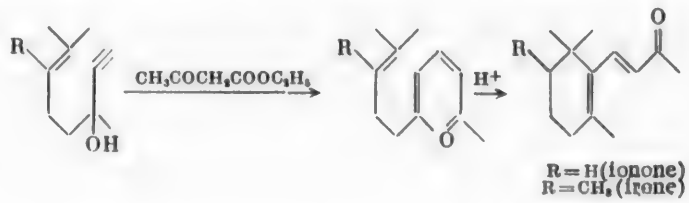
On the basis of linalool and using the same scheme for building up the isoprenoid chain (synthesis with acetoacetic ester or diketene, ethynylation, hydrogenation, and isomerization), nerolidol, farnesol, and geranylgeraniol were prepared.



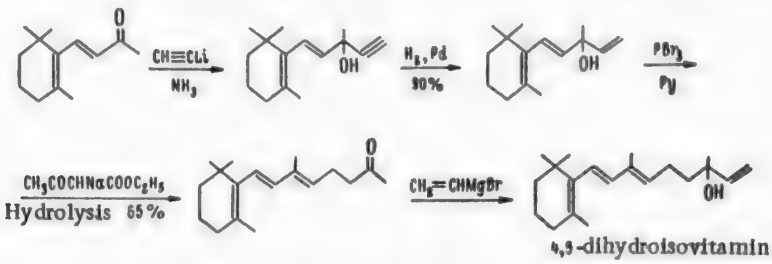


With appropriate changes (hydrogenation of the intermediate ketones), the same scheme was used for the synthesis of phytol, an important natural diterpene alcohol, forming part of the chlorophyll molecule.

The condensation of dehydrolinalool and 3-methyldehydrolinalool with acetoacetic ester yielded more than 50% of pseudoionone and pseudoirone, whose cyclization led to β-ionone and irone.



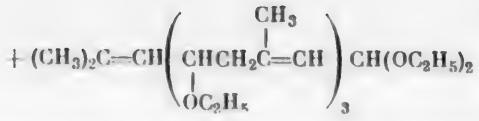
In a further series of reactions, it was possible to proceed from β-ionone to 4,5-dihydroisovitamin A.



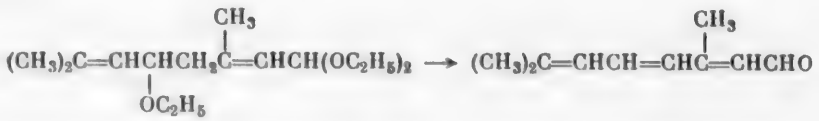
The synthesis of vitamin A itself by this method met with great difficulties and therefore a different and more convenient method was chosen, which was based on the condensation of acetals of aldehydes with 1-alkoxybutadienes, which had never been used for this purpose previously. Here addition proceeded in the 1,4-position and the chain was immediately lengthened (in the case of 1-ethoxyisoprene) by 5, 10, and even 15 carbon atoms [36].

$$(CH_3)_2C{=}CHCH(OC_2H_5)_2 \xrightarrow{CH_2{=}C(CH_3)CH{=}CHOC_2H_5} (CH_3)_2C{=}CHCH(OC_2H_5)CH_2C(CH_3){=}CHCH(OC_2H_5)_2 +$$

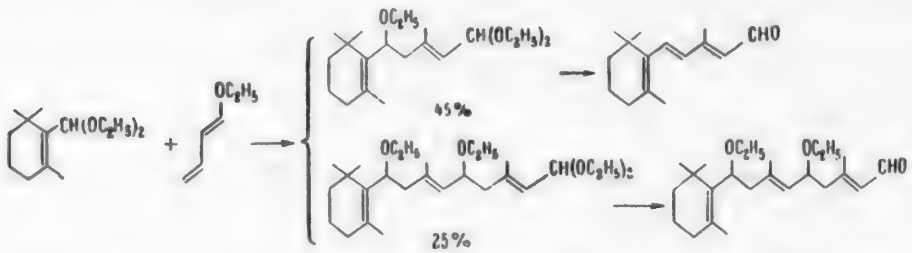
$$+ (CH_3)_2C{=}CH\left(CH(OC_2H_5)CH_2C(CH_3){=}CH\right)_2CH(OC_2H_5)_2 +$$



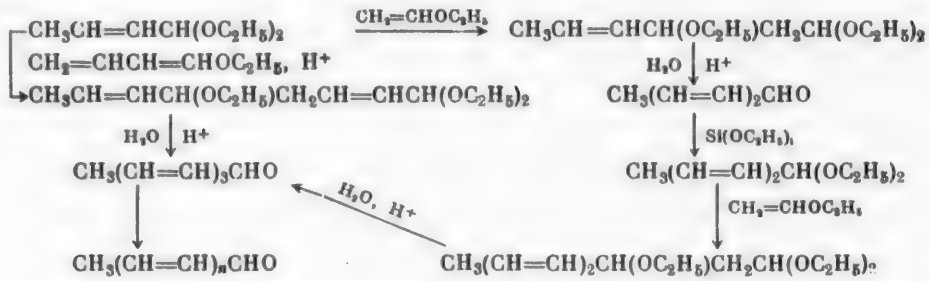
In an acid medium, the alkoxyacetals obtained were readily hydrolyzed and dehydrated with the formation of polyene aldehydes.



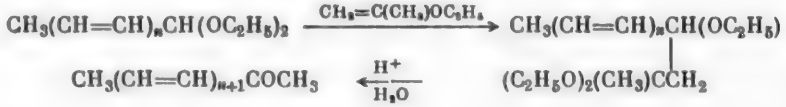
By this method, ionylundenacetaldehyde and vitamin A diethoxyaldehyde were prepared from cyclocitral.



In the case of crotonaldehyde acetal, by the gradual build-up of the chain by two carbon atoms (condensation with vinyl ethyl ether) or by four carbon atoms (condensation with 1-ethoxybutadiene), it was possible to synthesize practically any polyenal.



The condensation of acetals with isopropenyl ether by the same method yielded polyene ketones.



Other Works

Besides the work which may be assigned more or less definitely to one of the sections examined, I.N. Nazarov has left in his scientific legacy important investigations, which do not belong formally in the divisions covered here, but are quite valuable and sometimes are the beginning of new trends. Thus, the investigation of the electrophilic substitution of aromatic hydrocarbons was found to be very interesting. It was established that, in this process, the steric factor played an important role. Although chloromethylation of toluene (or of chloromethylbenzene) gave approximately equal amounts of ortho- and para-isomers, ethylbenzene gave 30% of the ortho-isomer, cumene gave 15%, while tert-butylbenzene did not form any at all. A similar, though less sharply expressed, rule is observed in nitration also. Toluene gave 67%, cumene, 40% and tert-butylbenzene, 12% of the ortho-isomer [37].

As indicated above, dihydroresorcinol and methyldihydroresorcinol are extremely promising starting materials for the synthesis of steroid compounds. However, conversions of the cyclohexanediones themselves, especially addition reactions, are also of considerable independent interest. Thus, in the presence of alkali, dimedone is capable of adding acrylic ester, acrylonitrile, maleic acid and other α,β-unsaturated compounds. Similar conversions were accomplished for dihydroresorcinol also. It is interesting to note that these condensations proceed despite the high enolizability of cyclohexanediones, which hinders the Michael reaction [38].

As can be seen from this short review, the investigations of Academician I.N. Nazarov are distinguished both by the breadth and the depth of the projects. Each of his new works and each trend was organically bound to the previous ones and stemmed from them logically. The investigations of I.N. on the chemistry of acetylene and vinylacetylene, the syntheses of physiologically active (anesthetic) substances, the syntheses of steroid compounds, and the investigations in the field of stereochemistry, diene synthesis, heterocyclic compounds, isoprenoids, cyclization, and isomeric conversions form part of the golden fund of Soviet chemistry.

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•A list of I.N. Nazarov's works, printed up to the middle of 1957, was presented in the profile "I.N. Nazarov" (Acad. Sci. USSR Press, Moscow, 1957). A list of the works issued after this date is being compiled and will be published in the book "I.N. Nazarov. Selected Works," which is being prepared for the press at present.

••Original Russian pagination. See C.B. translation.

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ANESTHETICS

XXIX. INVESTIGATION OF 1-PHENYL-3-METHYL-3-AMINOPROPANOLS AND THEIR ACYL DERIVATIVES

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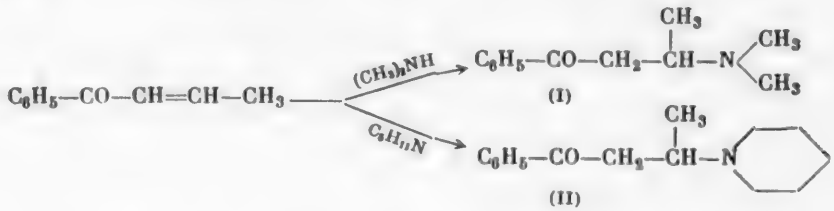
Over the last ten years we have systematically synthesized various esters of phenylalkyl-β-aminopropanols, among which were found substances with considerable physiological activity, and have elucidated the effect on the physiological activity of one or two methyl groups in the positions α and α,α to the hydroxyl group in the propanol chain [1, 2]. The effect of a methyl group in the β-position remained obscure.

We decided that it was necessary to synthesize and examine the esters of 1-alkyl-1-phenyl-3-methyl-3-aminopropan-1-ols, whose synthesis is published in the present communication. There is very little in the literature on this problem. The individual examples published are not systematic and are of a random nature [3-6].

Solitary papers [7, 8] report the positive effect of similar branching in the β-position on the physiological activity of certain amino ketones [8] and compounds of the monoalkylaminoethyl ester type, accompanied, it is true, by the negative property of these esters [7] of producing vasodilation.

The starting material used for the synthesis of the compounds listed was phenyl propylenyl ketone, which was treated with dimethylamine and piperidine to give β-dimethylaminobutyrophenone (I) and β-(N-piperidyl)-butyrophenone (II).

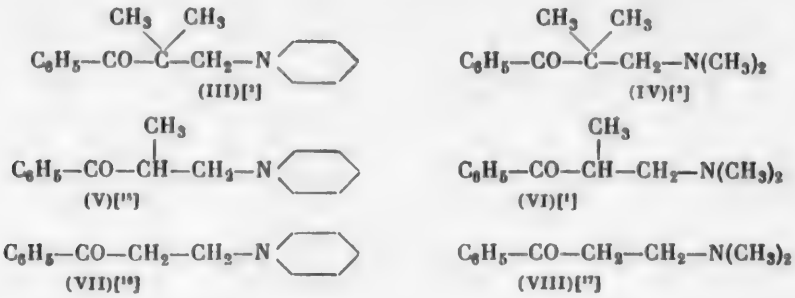


The amino ketones (I) and (II) obtained were unstable and decomposed considerably on distillation, even in vacuum. When hydrogenated over Ni—Pd-catalysts they were cleaved to a considerable degree to secondary amines and butyrophenone.

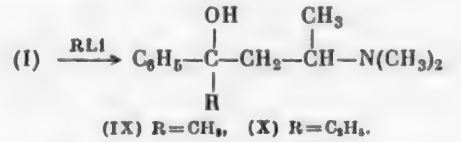
We previously noted this phenomenon with other examples [9]. The reduction of β-dimethylaminobutyrophenone (I) with aluminum isopropoxide, zinc and hydrochloric acid, sodium in aqueous alcohol and sodium amalgam (3 and 1%) was unsuccessful and also led to deamination products.

It is interesting that similar amino ketones, containing a CH_3 group in the position α to the CO group or without it (III—VIII) are reduced normally, giving high yields of the corresponding amino alcohols. Transfer of the methyl group from the α to the β-position leads to practically complete deamination of amino ketones (I) and (II) during reduction. The presence of two CH_3 groups in the α-position confers an increased stability on the

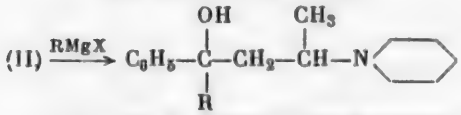
compounds: thus, ketones (III) and (IV) may be distilled without decomposition. We should note that their preparation gives comparatively worse yields than in the case of (I, II and V–VIII) [2].



The conversion of the β-aminobutyrophenones (I and II) into the corresponding tertiary amino alcohols was accomplished by means of organolithium and magnesium compounds.



(IX) R=CH_3, (X) R=C_2H_5.



(XI) R=CH_3 (α-isomer), (XII) (β-isomer),
(XIII) R=C_2H_5 (α-isomer), (XIV) (β-isomer).

These amino ketones behaved differently at this stage. With RMgX, β-dimethylaminobutyrophenone (I) gave the corresponding alcohols in insignificant yields, due, as our experiments showed, to enolization of (I) under the action of Grignard reagents.* The use of CH_3Li and C_2H_5Li increased the yield to 28%.

The other ketone, β-(N-piperidyl)-butyrophenone (II), reacted with Mg-organic reagents in the usual way, giving 63-70% yields of the desired amino alcohols. In accordance with theory, in each case it was possible to isolate two diastereoisomeric forms of the amino alcohols (XI–XIV), which we provisionally designated as α- and β-forms. All those compounds whose hydrochlorides melted at lower temperatures than the corresponding hydrochlorides of the β-isomers, we designated α-isomers. Some of the experimental results are presented in Table 1.

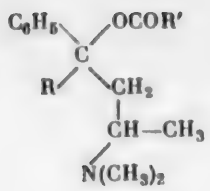
As the data in Table 1 show, the n_D values of the α-isomers are higher than those of the corresponding β-isomers, the melting points of the hydrochlorides of the α-isomers are lower than those of the β-isomers and the latter are less soluble in water. In the reactions with most of the amino ketone bases, the yields of the β-isomers were 1.7-2.5 times greater than those of the corresponding α-isomers, however, it was possible to increase the yield of the latter if the amino ketone hydrochloride (II) was used.

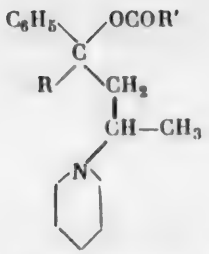
The amino alcohols obtained were esterified with benzoyl, cinnamyl, β-phenoxypropionyl and phenoxyacetyl chlorides under various conditions. Despite its apparent simplicity, this stage of the reaction often involved great difficulties. In a series of cases it was impossible to isolate crystalline hydrochloride of the esters by the usual methods. Successful results could only be obtained after prolonged drying in vacuum.

Some of the esters were also prepared by the action of the acid chlorides on the sodium and magnesium alcoholates (see scheme, below).

The yields of the esters obtained (as hydrochlorides) are presented in Table 2.

*L.N. Nazarov et al. recently described examples of the high tendency for enolization in the γ-piperidone series under Grignard reaction conditions [10].





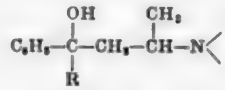
(XV) R = CH_3; R′ = C_6H_5
(XVI) R = CH_3; R′ = $C_6H_5CH{=}CH$
(XVII) R = CH_3; R′ = $C_6H_5OCH_2$
(XVIII) R = CH_3; R′ = $C_6H_5OCH_2CH_2$
(XIX) R = C_2H_5; R′ = C_6H_5
(XX) R = C_2H_5; R′ = $C_6H_5CH{=}CH$

(XXI) R = CH_3 (α-isomer); R′ = C_6H_5
(XXII) R = CH_3 (β-isomer); R′ = C_6H_5
(XXIII) R = CH_3 (α-isomer); R′ = $C_6H_5OCH_2$
(XXIV) R = CH_3 (β-isomer); R′ = $C_6H_5OCH_2$
(XXV) R = CH_3 (α-isomer); R′ = $C_6H_5OCH_2CH_2$
(XXVI) R = CH_3 (β-isomer); R′ = $C_6H_5OCH_2CH_2$
(XXVII) R = C_2H_5 (α-isomer); R′ = C_6H_5
(XXVIII) R = C_2H_5 (β-isomer); R′ = C_6H_5
(XXIX) R = C_2H_5 (α-isomer); R′ = $C_6H_5OCH_2$
(XXX) R = C_2H_5 (β-isomer); R′ = $C_6H_5OCH_2$
(XXXI) R = C_2H_5 (α-isomer); R′ = $C_6H_5OCH_2CH_2$
(XXXII) R = C_2H_5 (β-isomer); R′ = $C_6H_5OCH_2CH_2$

Analysis of the experimental material shows a characteristic trend in the behavior of the starting components in the esterification reaction.

Among the β-(N-piperidyl)-propanols (judging by the amount of the original alcohols recovered), in certain cases the α-isomers are esterified more readily than the corresponding β-isomers, although the average yield of esters of the α-isomers is 38% and of the β-isomers, 49%. The benzoyl and also the phenoxyacetyl radicals replace the hydroxyl hydrogen with more difficulty than the β-phenoxypropionyl radical. The two types of aminopropanols investigated, both with the dimethylamino and the piperidino residues (IX–XIV), substituted with a methyl in position 1, are esterified more readily than their 1-ethyl substituted homologs.

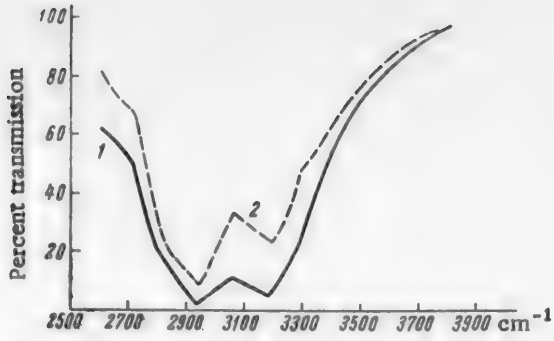
TABLE 1



Compound No.	R	N<	Form of isomer	n_D^{20}	M.p. of hydrochloride	Isomer yield (in %)		Notes
						calc. on original amino ketone	calc. on amino ketone hydrochloride	
(XI)	CH_3	$C_5H_{10}N$	α	1.5220	159°	17.1	—	With CH_3MgI instead of CH_3MgBr, yield of (XI) and (XII) fell to 6%
(XII)	CH_3	$C_5H_{10}N$	β	1.5177	230	45.3	—	
(XIII)	C_2H_5	$C_5H_{10}N$	α	1.5195	187—188	25.5	38.6	
(XIV)	C_2H_5	$C_5H_{10}N$	β	1.5157	234—235	44.5	28.6	
(IX)	CH_3	$N(CH_3)_2$	—	—	182—183	—	—	CH_3Li was used
(X)	C_2H_5	$N(CH_3)_2$	—	—	168—170	—	—	C_2H_5Li was used

The phenomena described above, especially the difficulties in achieving esterification, apparently may be explained by steric hindrance. The tendency for the formation of an intramolecular hydrogen bond is an indication of the proximity of the hydroxyl group and the substituted amino group and, consequently, the other groupings at the β-carbon atom (relative to the carbon atom not bearing the hydroxyl group).* Actually, for both of the diastereoisomeric 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propanols (XI and XII) in carbon tetrachloride solution

*The authors would like to thank G.I. Samokhvalov and L.V. Luk'yanova for help in plotting and interpreting the infrared absorption spectra.



Infrared absorption spectra of 1,3-dimethyl-1-phenyl-(N-piperidyl)-propan-1-ols in carbon tetrachloride (0.5-1% solution): 1) (XI) α-form; 2) (XII) β-form.

a displacement in vibration frequency toward longer wavelengths and shorter frequencies is observed and the frequencies equal 3190 cm^{-1} for the α-form (XI) and 3195 cm^{-1} for the β-form (XII). At the given solution concentration, the substances may be considered as unassociated and their molecules as single, monomeric and surrounded by solvent molecules. Likewise, the effect of single molecules on each other is excluded. Consequently, the displacement of the vibration frequency of the hydroxyl group is caused solely by the presence of an intramolecular hydrogen bond and not by intermolecular bonding. The presence of steric hindrance is particularly strongly expressed in benzoylation, where the relatively large volume of the phenyl nucleus with the carboxyl group causes the greatest difficulty in the approach of the reacting molecules. In addition, the size of the alkyl group on the carbon atom not bearing the hydroxyl group has a considerable effect on the ease of esterification as is observed, for example, in going from methyl to ethyl homologs.

The hydrochlorides of the esters were colorless crystalline substances which, as a rule, were soluble in water and insoluble in ether.•

TABLE 2

Ester No.	Amount of alcohol recovered (in %)	Yield (in %)	Ester No.	Amount of alcohol recovered (in %)	Yield (in %)
(XV)	—	50 (isolated in the form of a base)	(XXIV)	29.5	20.0
(XVI)	—	56	(XXV)	—	54.3
(XVII)	—	53	(XXVI)	—	84
(XVIII)	—	53.7	(XXVII)	—	29.9
(XIX)	—	Low	(XXVIII)	—	68.8
(XX)	—	Low (~4%)	(XXIX)		42.7
(XXI)	—	38.7	(XXX)	22.5	14.2
(XXII)	14.1	26.5	(XXXI)	—	40.5
(XXIII)		24.7	(XXXII)	—	75

EXPERIMENTAL••

Starting materials. Crotonic acid was prepared by Scheibler's method [11] in 65% yield and had m.p. 67-70°. Crotonyl chloride••• was prepared by heating crotonic acid with thionyl chloride. The yield was 88% and the b.p. 37-40° (33 mm). Phenyl propenyl ketone was prepared by Fuson's method [12] in 70% yield instead of 61% reported by the author, due to longer irradiation with the mercury lamp. The b.p. was 95-100° (2 mm).

β-(N-Piperidyl)-butyrophenone (II) with m.p. 39-40° was prepared by Pohland and Sullivan's method [13] in 79% yield.

β-Dimethylaminobutyrophenone (I) was prepared by Pohland and Sullivan's method. It could not be distilled (the yield was 84%). The hydrochloride of the amino ketone had m.p. 130-132° [13].

•The substances were tested for physiological activity in the Ordzhonikidze Sci.-Res. Inst. of Chem. Pharmaceutics. The results of the tests will be published.

••The piperidylpropanols were isolated by Ch'ang Ch'ung Kwang.

•••This acid chloride was prepared by Fuson [12] in 86% yield in petroleum ether.

Reduction of β-dimethylaminobutyrophenone. 1.5 g of β-dimethylaminobutyrophenone in 20 ml of anhydrous alcohol was hydrogenated in the presence of 1 g of Raney nickel catalyst for four hours. 260 ml of hydrogen was absorbed instead of the 210 ml calculated theoretically. The catalyst was filtered off, the alcohol evaporated, the residue acidified with hydrochloric acid (1:1) and the neutral products extracted with ether and dried over magnesium sulfate. The ether was removed and the residue (0.6 g) vacuum distilled and converted to a semicarbazone, which melted at 185-187° [14].

1,3-Dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XI and XII). 23.1 g of β-(N-piperidyl)-butyrophenone was added over a period of one hour with stirring and cooling to −20° and in the range 20-3° to methylmagnesium bromide (from 7.2 g of magnesium and the corresponding amount of methyl bromide). On the following day, the reaction mixture was decomposed with 300 ml of hydrochloric acid (1:1) and ice. The precipitate was filtered off, washed on the filter and converted into the base, which was extracted with ether. The ether extract was dried with magnesium sulfate, the ether distilled off and the product vacuum distilled. We obtained 11.2 g (45.3%) of the β-form of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XII) with b.p. 113.5-114° (0.6 mm), $n^{20}D$ 1.5177.

Found %: N 5.69, 5.08. $C_{16}H_{25}ON$. Calculated %: N 5.67.

The hydrochloride melted at 230° (from alcohol).

Found %: C 67.66, 67.71; H 8.92, 9.32; N 4.86, 4.73. $C_{16}H_{25}ON \cdot HCl$. Calculated %: C 67.75; H 9.18; N 4.93.

After separation of the neutral products, the aqueous acid solution was treated with sodium hydroxide solution and extracted several times with ether. The ether extract was dried, the ether removed and the residue vacuum distilled. We obtained 4.23 g (17.1%) of the α-form of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XI) with b.p. 118-120° (0.6 mm), $n^{20}D$ 1.5220.

Found %: N 5.30, 5.28. $C_{16}H_{25}ON$. Calculated %: N 5.67.

The hydrochloride melted at 159° (from alcohol).

Found %: C 67.87, 68.00; H 9.17, 9.41; N 5.10, 5.07. $C_{16}H_{25}ON \cdot HCl$. Calculated %: C 67.75; H 9.18; N 4.93.

When methylmagnesium iodide was used, the amino alcohols described above were obtained in 5-6% yield.

1-Ethyl-1-phenyl-3-methyl-2-(N-piperidyl)-propan-1-ol (XIII and XIV). a) From the amino ketone hydrochloride. 26.7 g of β-(N-piperidyl)-butyrophenone hydrochloride was gradually added at −10 to −5° with continuous stirring to the Grignard reagent prepared from 7.2 g of magnesium and 36.3 g of ethyl bromide in 50 ml of ether. The reaction products were worked up as in the previous case. We obtained 7.4 g (28.6%) of the β-form of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XIV) with b.p. 136-137° (1.5 mm), $n^{20}D$ 1.5177 (isolated from the difficultly soluble hydrochloride).

Found %: N 5.05, 5.16. $C_{17}H_{27}ON$. Calculated %: N 5.35.

The hydrochloride melted at 234-235° (from alcohol).

Found %: C 68.55, 68.90; H 9.57, 9.47; N 4.40, 4.37. $C_{17}H_{27}ON \cdot HCl$. Calculated %: C 68.60; H 9.42; N 4.70.

After the addition of sodium hydroxide, the aqueous acid solution yielded 10.1 g (38.6%) of the α-form of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XIII) with b.p. 135-136° (1.5 mm), $n^{20}D$ 1.5195.

Found %: N 5.49, 5.37. $C_{17}H_{27}ON$. Calculated %: N 5.35.

The hydrochloride had m.p. 187-188° (from alcohol).

Found %: C 68.34, 68.91; H 9.16, 9.06; N 4.42, 4.46. $C_{17}H_{27}ON \cdot HCl$. Calculated %: C 68.6; H 9.42; N 4.70.

b) From the amino ketone base. From 23.1 g of β-(N-piperidyl)-butyrophenone base and the Grignard reagent, prepared from 7.2 g of magnesium and 36.3 g of ethyl bromide in 50 ml of ether, we isolated 11.5 g (44.1%) of the β-form of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XIV) with b.p. 123-124° (0.5 mm),

$n^{20}D$ 1.5157 (from the difficultly soluble hydrochloride, which melted at 233-234°). The acid solution yielded 6.7 g (25.5%) of the α-form of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XIII) with b.p. 135-136° (1.5 mm), $n^{20}D$ 1.5194; the hydrochloride melted at 187-188°.

1,3-Dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (IX). a) With methyllithium. With cooling (−5 to −20°) and vigorous stirring, 24.4 g of β-dimethylaminobutyrophenone was added dropwise to 4.3 g of lithium in 100 ml of absolute ether and 47.7 g of freshly distilled methyl iodide. On the following day, the reaction mixture was hydrolyzed with pieces of ice and hydrochloric acid (1:1), being made acid to Congo. The neutral products were extracted with ether and isolated. The aqueous layer was treated with ammonia and then sodium carbonate and extracted several times with ether. The ether solution was dried with magnesium sulfate and the product vacuum distilled. We obtained 7.5 g (28.3%) of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (IX) with b.p. 110-120° (3-4 mm).

Found %: N 6.68, 6.47. $C_{13}H_{21}ON$. Calculated %: N 6.74.

The picrate melted at 168-169°.

Found %: N 13.18, 13.01. $C_{13}H_{21}ON \cdot C_6H_2OH(NO_2)_3$. Calculated %: N 12.82.

b) With methylmagnesium iodide. 3 g of β-dimethylaminobutyrophenone was added dropwise at 0-6° with stirring to the Grignard reagent prepared from 0.46 g of magnesium and 10 g of methyl iodide in 15 ml of ether. The mixture was stirred for one hour at room temperature and then at the boiling point of the ether on the following day. 960 ml of gas was collected in the gasometer. The reaction mixture was acidified with hydrochloric acid (1:1) with cooling and the neutral products extracted with ether. The aqueous solution of the nitrogenous base salts was saturated with sodium hydroxide solution and extracted with ether. The ether extracts were dried with magnesium sulfate, the ether removed and the residue (0.6 g) converted into the hydrochloride. We obtained 0.4 g of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol hydrochloride with m.p. 182-183° (from alcohol).

Found %: C 64.29, 64.59; H 9.19, 9.16; N 5.80, 5.58. $C_{13}H_{21}ON \cdot HCl$. Calculated %: C 64.4; H 9.10; N 5.75.

The gas was analyzed with an Orsat apparatus and shown to have the following composition: CO_2 − 9.8%, O_2 − 4%, CH_4 − 26.6%, which corresponds to 65% enolization of the β-dimethylaminobutyrophenone.

1-Ethyl-1-phenyl-3-dimethylaminopropan-1-ol (X). 20.3 g of β-dimethylaminobutyrophenone in 40 ml of ether was added dropwise at 2-6° to ethyllithium, prepared in the usual way from 5.82 g of lithium and 46 g of ethyl bromide in 40 ml of absolute ether. The following day, the reaction mixture was treated as described in the previous experiment. After removal of the ether from the ether solution of the base, the residue was vacuum distilled. We collected 5.4 g (23.1%) of a substance with b.p. 120-130° (3-4 mm). The product was dissolved in chloroform and treated with dry hydrogen chloride. We obtained 1-ethyl-1-phenyl-3-methyl-3-dimethylaminopropan-1-ol hydrochloride with m.p. 168-170° (from alcohol).

Found %: C 65.51, 65.15; H 8.64, 8.46; N 5.48, 5.37. $C_{14}H_{23}ON \cdot HCl$. Calculated %: C 65.30; H 9.40; N 5.40.

Part of the amino alcohol hydrochloride (m.p. 168-170°) was converted in the usual way into the base, 1-ethyl-1-phenyl-3-methyl-3-dimethylaminopropan-1-ol.

Found %: N 6.04, 6.00. $C_{14}H_{23}ON$. Calculated %: N 6.33.

The benzoate of the α-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXI). Into a 50 ml, flat-bottomed flask was placed 2.47 g of the α-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol and 10 g of benzoyl chloride. The following day, the product was precipitated with absolute ether and recrystallized from acetone and then from acetone and chloroform, when it melted at 157-158°. We obtained 1.5 g (38.7%) of the hydrochloride of the benzoate of the α-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXI).

Found %: N 3.96, 3.80. $C_{23}H_{29}O_2N \cdot HCl$. Calculated %: N 3.61.

The benzoate of the β-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXII). A mixture of 4.94 g of the β-isomer of 1,3-dimethyl-3-(N-piperidyl)-propan-1-ol and 20 g of freshly distilled benzoyl chloride was kept at room temperature for 20 hours. The product was then precipitated with ether, filtered off,

and recrystallized from a mixture of acetone and chloroform. We recovered 0.8 g of the hydrochloride of the starting amino alcohol with m.p. 225°. Ether was added to the mother solution; the product isolated was recrystallized several times from acetone and chloroform. We obtained 2.05 g (26.5%) of the hydrochloride of the benzoate of the β-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXII) with m.p. 112-113°.

Found %: N 3.70, 3.46. $C_{23}H_{29}O_2N \cdot HCl$. Calculated %: N 3.61.

The phenoxyacetate of the α-isomer of 1-phenyl-1,3-dimethyl-3-(N-piperidyl)-propan-1-ol (XXIII). 3.4 g of phenoxyacetyl chloride in 10 ml of ether was slowly added with cooling to 2.47 g of the α-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol, dissolved in 10 ml of absolute ether. An oily product precipitated which, after standing for three days, was washed with absolute ether until the smell of the acid chloride disappeared. The oily product obtained was dried in a vacuum desiccator with pumping for 45 hours. We obtained 1.03 g (24.7%) of the hydrochloride of the phenoxyacetate of the α-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXIII) as an amorphous mass. The form changed at 90°, but no sharp melting point was observed.

Found %: C 63.76, 68.83; H 7.95, 7.95; N 3.20, 3.10. $C_{24}H_{31}O_3N \cdot HCl$. Calculated %: C 69.00; H 7.69; N 3.36.

The phenoxyacetate of the β-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXIV). A mixture of 4.9 g of the β-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol and 6.8 g of phenoxyacetyl chloride in 30 ml of absolute ether was left for a day. The precipitate was washed with ether and recrystallized from chloroform. We recovered 1.67 g of the hydrochloride of the starting amino alcohol (m.p. 230°), which did not depress the melting point of an authentic sample. The chloroform mother solution was evaporated to dryness and the residue recrystallized several times from acetone and chloroform. We obtained 1.7 g (20.6%) of the hydrochloride of the phenoxyacetate of the β-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXIV) with m.p. 149-150°.

Found %: C 68.76, 68.78; H 7.91, 7.79; N 3.32, 3.30. $C_{24}H_{31}O_3N \cdot HCl$. Calculated %: C 69.00; H 7.69; N 3.36.

The β-phenoxypropionate of the α-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXV). 2.4 g of the α-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol, 3 g of β-phenoxypropionyl chloride and 20 ml of absolute ether were used. The mixture was left for a day and then the oil separated was washed several times with ether, when it crystallized. Several recrystallizations from acetone yielded 2.28 g (54.3%) of the hydrochloride of the β-phenoxypropionate of the α-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXV) with m.p. 146-147°.

Found %: C 69.88, 69.82; H 7.77, 8.02; N 3.46, 3.70. $C_{25}H_{33}O_3N \cdot HCl$. Calculated %: C 69.60; H 7.88; N 3.24.

The β-phenoxypropionate of the β-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXVI). By the procedure described in the previous experiment, from 2.47 g of the β-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol and 3 g of β-phenoxypropionyl chloride in 10 ml of absolute ether, we obtained 3.62 g (84%) of the hydrochloride of the β-phenoxypropionate of the α-isomer of 1,3-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (XXVI) with m.p. 168-168.5° (from chloroform and acetone).

Found %: C 69.30, 69.33; H 7.98, 8.08; N 3.38, 3.57. $C_{25}H_{33}O_3N \cdot HCl$. Calculated %: C 69.60; H 7.88; N 3.24.

The benzoate of the α-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXVII). 2.3 g of the hydrochloride of the α-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol was gradually added to a solution of methylmagnesium iodide (0.72 g of magnesium and 4.74 g of methyl iodide in 20 ml of absolute ether). Stirring was continued for a further one hour, after which 3.5 g of benzoyl chloride in 10 ml of absolute ether was slowly added through a dropping funnel with stirring and cooling in ice water. The dark-brown oil which precipitated gradually solidified. The mixture was stirred for one hour and left overnight, after which it was decomposed with 20 ml of cooled hydrochloric acid (1:1). The white precipitate was filtered off and recrystallized several times from chloroform with acetone. We obtained 0.93 g (29.9%) of the hydrochloride of the benzoate of the α-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXVII) with m.p. 155-156°.

Found %: N 3.63, 3.56. $C_{24}H_{31}O_2N \cdot HCl$. Calculated %: N 3.48.

After separation of the neutral products, the acid solution was made alkaline and extracted with ether. The extract was dried and dry hydrogen chloride passed through it. We isolated 0.42 g of a benzoate hydrochloride with m.p. 151-153°, which did not depress the melting point of the sample described above.

The benzoate of the β-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXVIII). Under the conditions described above, from 2.31 g of the hydrochloride of the β-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol, 3.5 g of benzoyl chloride and the Grignard reagent prepared from 0.72 g of magnesium and 4.74 g of methyl iodide in 20 ml of ether, we obtained 2.15 g of the hydrochloride of the benzoate of the β-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXVIII) with m.p. 202-203° (from chloroform). The yield was 2.43 g (78%).

Found %: N 3.50, 3.54. $C_{24}H_{31}O_2N \cdot HCl$. Calculated %: N 3.48.

The phenoxyacetate of the α-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXIX). 3 g of phenoxyacetyl chloride in 10 ml of ether was slowly added to 2.51 g of the α-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol, dissolved in 10 ml of absolute ether. A precipitate covered with oil formed immediately. The mixture was left for two days. The precipitate was washed with absolute ether until the smell of the acid chloride disappeared and twice recrystallized from acetone. We obtained 1.77 g (42.7%) of the hydrochloride of the phenoxyacetate of the α-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXIX) with m.p. 151-152°.

Found %: C 69.86, 69.72; H 8.18, 7.98; N 3.59, 3.69. $C_{25}H_{33}O_3N \cdot HCl$. Calculated %: C 69.60; H 7.88; N 3.24.

The phenoxyacetate of the β-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXX). 5 g of phenoxyacetyl chloride was added to 2.61 g of the β-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol, heated on a water bath. The following day, absolute ether was added and the precipitate which formed was separated, washed with ether and recrystallized from acetone. 0.67 g of the hydrochloride of the starting amino alcohol (m.p. 228-229°) was recovered. A small amount of absolute ether was added to the mother solution and the product which precipitated was recrystallized from acetone. We obtained 0.61 g (14.2%) of the hydrochloride of the phenoxyacetate of the β-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXX) with m.p. 132-133°.

Found %: C 69.33, 69.35; H 7.96, 8.04; N 3.30, 3.57. $C_{25}H_{33}O_3N \cdot HCl$. Calculated %: C 69.60; H 7.88; N 3.24.

The β-phenoxypropionate of the α-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXXI). 5 g of β-phenoxypropionyl chloride was added to 2.61 g of the α-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol. The mixture was left for a day and the solid mass covered with absolute ether and ground for 0.5 hour. The ether insoluble part was filtered off and recrystallized twice from acetone. We obtained 1.8 g (40.5%) of the hydrochloride of the β-phenoxypropionate of the α-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXXI) with m.p. 155-157° after several recrystallizations from acetone.

Found %: C 70.20, 70.27; H 7.69, 7.97; N 3.44. $C_{26}H_{35}O_3N \cdot HCl$. Calculated %: C 70.00; H 8.06; N 3.14.

The β-phenoxypropionate of the β-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXXII). 7 g of β-phenoxypropionyl chloride was added to 5.22 g of the β-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol. The mixture heated up to 70°. The reaction mixture was left for a week, then washed with absolute ether until the smell of the acid chloride disappeared and recrystallized several times from chloroform and acetone. We obtained 6.69 g (75%) of the hydrochloride of the β-phenoxypropionate of the β-isomer of 1-ethyl-1-phenyl-3-methyl-3-(N-piperidyl)-propan-1-ol (XXXII) with m.p. 169-170°.

Found %: C 70.17, 70.11; H 7.71, 7.89; N 3.28, 3.57. $C_{26}H_{35}O_3N \cdot HCl$. Calculated %: C 70.00; H 8.06; N 3.14.

The benzoate of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (XV). 0.187 g of sodium was dispersed in 15 ml of dioxane at 80-100° with vigorous mixing. The reaction flask was then placed in a cooling mixture and 2 g of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol added in three portions. The mixture was stirred for 45 minutes. The following day 1.25 g of freshly distilled benzoyl chloride was added dropwise

with cooling. The mixture was heated for three hours at 90-100°, cooled and acidified, the neutral products extracted with ether and the aqueous solution of nitrogen base salts made alkaline and extracted with ether. The ether extracts were dried with magnesium sulfate, the ether removed and the product vacuum distilled. We obtained 1.5 g (50%) of the benzoate of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (XV) with b.p. 95-100° (0.02 mm).

Found %: N 5.01, 5.09. $C_{20}H_{25}O_2N$. Calculated %: N 4.50.

The hydrochloride of the benzoate of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol melted at 154-156° (from acetone).

Found %: C 69.35, 69.35; H 7.75, 7.73; N 3.90, 4.06. $C_{20}H_{25}O_2N \cdot HCl$. Calculated %: C 69.00; H 7.54; N 4.00.

Cinnamyl ester of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (XVI). 2 g of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol, 2.5 g of cinnamyl chloride and 15 ml of anhydrous benzene were mixed. On the following day, the reaction mixture was heated with 30 ml of absolute ether for 30 minutes. The ether was decanted, a new portion of ether added and the crystalline product carefully ground under the ether, then separated and recrystallized from chloroform. We obtained 2 g (55.6%) of the hydrochloride of the cinnamate of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (XVI) with m.p. 205-206°.

Found %: N 3.57, 3.73. $C_{22}H_{27}O_2N \cdot HCl$. Calculated %: N 3.74.

The phenoxyacetate of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (XVII). By the procedure described in the previous experiment, from 2.07 g of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 2 g of phenoxyacetyl chloride in 15 ml of benzene, we obtained 2 g (53%) of the hydrochloride of the phenoxyacetate of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (XVII) with m.p. 150-152° (from acetone).

Found %: N 3.83, 3.53. $C_{21}H_{27}O_3N \cdot HCl$. Calculated %: N 3.71.

The β-phenoxypropionate of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (XVIII). Under the conditions described above, from 2.07 g of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol, 2.5 g of β-phenoxypropionyl chloride and 20 ml of absolute ether, we obtained 2.1 g (53.7%) of the hydrochloride of the β-phenoxypropionate of 1,3-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol (XVIII) with m.p. 175-177° (from acetone).

Found %: N 3.57, 3.93. $C_{22}H_{29}O_3N \cdot HCl$. Calculated %: N 3.58.

The benzoate of 1-ethyl-1-phenyl-3-methyl-3-dimethylaminopropan-1-ol (XIX). A mixture of 0.7 g of 1-ethyl-1-phenyl-3-methyl-3-dimethylaminopropan-1-ol, 0.95 g of benzoyl chloride and 4 ml of anhydrous benzene was kept at room temperature for 15 hours and then heated on a water bath for one hour at 80-90°. Absolute ether was added to the cooled mixture until the oil had precipitated completely and the latter was washed with ether until the smell of the acid chloride disappeared. The product obtained (0.9 g) was converted into the base in the usual way. We prepared the picrate of the benzoate of 1-ethyl-1-phenyl-3-methyl-3-dimethylaminopropan-1-ol (XIX) with m.p. 170-171° (from acetone).

Found %: N 10.43, 10.65. $C_{21}H_{27}O_2N \cdot C_6H_2OH(NO_2)_3$. Calculated %: N 10.01.

The hydrochloride of benzoate (XIX) could not be obtained in the crystalline form.

The cinnamic ester of 1-ethyl-1-phenyl-3-methyl-3-dimethylaminopropan-1-ol (XX). By the procedure described in the previous experiment, from 2 g of 1-ethyl-1-phenyl-3-methyl-3-dimethylaminopropan-1-ol, 3.6 g of cinnamyl chloride, and 30 ml of anhydrous benzene we obtained the cinnamate of 1-ethyl-1-phenyl-3-methyl-3-dimethylaminopropan-1-ol (XX) with b.p. 175-180° (5 mm) and this was directly converted into the hydrochloride (0.15 g), which melted at 242-244° (from acetone).

Found %: N 4.00, 4.10. $C_{23}H_{29}O_2N \cdot HCl$. Calculated %: N 3.61.

SUMMARY

For a comparative pharmacological investigation we synthesized a series of new esters of 1-alkyl-1-phenyl-3-methyl-3-aminopropanols with dimethylamino and piperidino residues as the nitrogenous components. A method of synthesizing the main intermediate products, amino alcohols and amino ketones, was developed.

As a special investigation of the infrared absorption spectra showed, some of the amino alcohols have strongly expressed intramolecular hydrogen bonding.

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SYNTHESIS OF THE SIMPLEST ANALOGS OF CORTICOSTEROIDS

VII.* INTRODUCTION OF A DIHYDROXYACETONE SIDE CHAIN BY HYDRATION OF ACETYLENE ALCOHOLS

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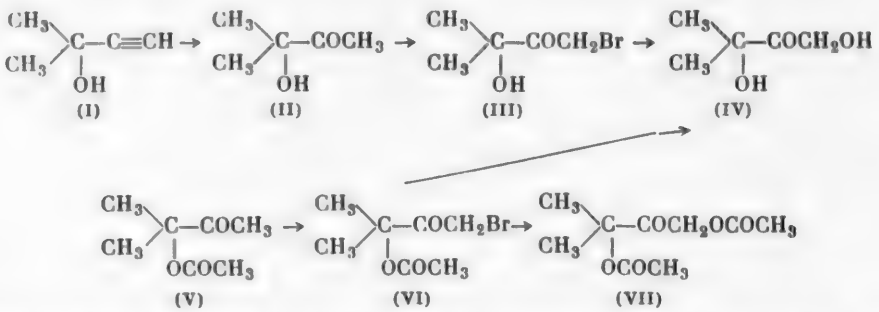
We previously described [1] the bromohydrin, dibromoketol and glycidol methods of introducing oxidized side chains into cyclic compounds. It also seemed interesting to study the method of introducing a dihydroxyacetone side chain based on the hydration of acetylene alcohols, which have been studied in our laboratory for a number of years.

When our investigations were complete, several papers [2-4] appeared devoted to the synthesis of the simplest analogs of cortisone in which the same method of introducing a dihydroxyacetone side chain was used. However, in a series of cases the yields of intermediate and final products were lower than ours and therefore, we consider it necessary to publish the results of our work in this direction.

We began the investigation with the most readily available acetylene alcohol, dimethylethynylcarbinol (I), which was obtained in high yield by the Favorskii condensation of acetylene with acetone [5].

Hydration of carbinol (I) in the presence of mercuric sulfate gave a high yield of dimethylacetylcarbinol (II) [6], which reacted with dioxane dibromide to form bromoacetyldimethylcarbinol (III). The action of potassium hydroxide in alcohol solution on the latter formed dimethylhydroxyacetylcarbinol (IV).

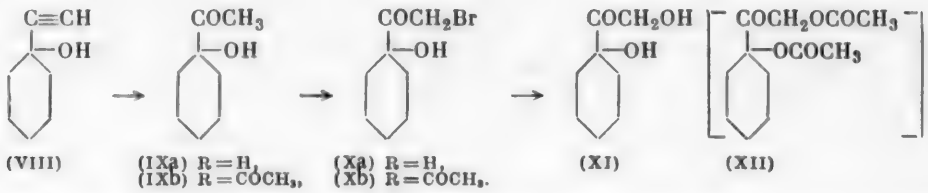


The action of dioxane dibromide on the acetate of dimethylacetylcarbinol (V) [6] gave a 61% yield of the acetate of ω-bromoacetyldimethylcarbinol (VI). When the latter was treated with potassium hydroxide in alcohol

*Communication I in this series was published in J. Gen. Chem. 26, 1186 (1956). Communication II, labeled I in error, was published in J. Gen. Chem. 28, 1458 (1958). Communication III, labeled II in error, was published in J. Gen. Chem. 28, 1791 (1958). Communication IV was published in J. Gen. Chem. 28, 1805 (1958). Communication V was published in J. Gen. Chem. 28, 2199 (1958). Communication VI, labeled III in error, was published in J. Gen. Chem. 28, 2187 (1958). (See C.B. translations.)

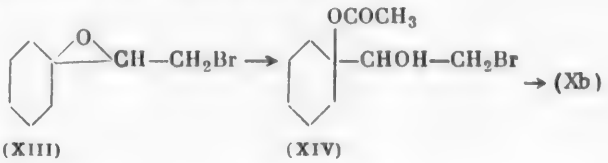
solution, it was converted into dimethylhydroxyacetylcarbinol (IV) in 63% yield and acetolysis with potassium acetate in methanol gave the diacetate of dimethylhydroxyacetylcarbinol (VII) in 70% yield.

Hydration with mercuric sulfate in methanol of 1-ethynylcyclohexanol (VIII) [7], synthesized in high yield from cyclohexanone and acetylene by the Favorskii reaction, yielded 1-acetylcyclohexanol (IXa) [2, 3]. Treatment of the latter with acetic anhydride formed the acetate of 1-acetylcyclohexanol (IXb). Bromination of 1-acetylcyclohexanol (IXa) with dioxane dibromide in dioxane gave 1-bromoacetylcyclohexanol (Xa). Saponification of the bromide (Xa) with caustic alkali in an aqueous chloroform solution formed 1-hydroxyacetylcyclohexanol (XI) [2, 3].



(VIII) (IXa) R = H, (IXb) R = COCH3, (Xa) R = H, (Xb) R = COCH3. (XI) (XII)

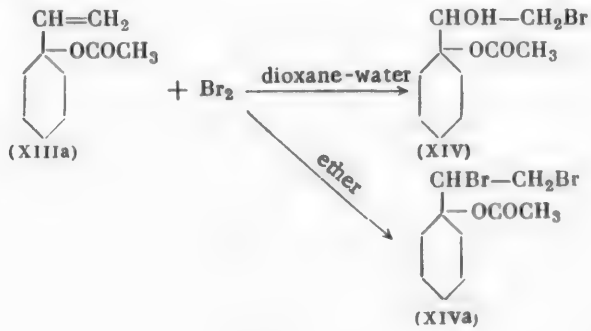
Bromination of the acetate (IXb) with dioxane dibromide in ether yielded the acetate of 1-bromoacetylcyclohexanol (Xb) [1]. Acetolysis of the bromide (Xb) with potassium acetate in anhydrous methanol formed the diacetate (XII), which could not be isolated in the pure form. Bromination of the α-ketol (IXa) with dioxane dibromide in ether, with bromine in chloroform or with bromine in acetic acid gave the bromide (Xa), but in lower yields. Here, together with the bromide (Xa), a crystalline isomeric bromide [2] with m.p. 118-118.5° was formed and its structure has not been established. We also prepared the acetate of the bromide (Xb) with m.p. 34-35° [1, 2] by another method, starting from the bromooxide [1] (XIII). Acetolysis of the latter with acetic acid gave the known [1] crystalline bromohydrin acetate (XIV), whose oxidation with chromium trioxide in acetic acid led to the formation of bromide (Xb), as was shown previously [1].



(XIII) (XIV)

It is interesting to note that the bromohydrin acetate (XIV) was obtained in the bromination of the acetate of 1-vinylcyclohexanol (XIIIa) with bromine in aqueous dioxane (i.e., conditions favorable to bromination of the double bond). Apparently, the tertiary acetoxy conjugated with the double bond facilitates the addition to the latter of the elements of hypobromous acid, while the free tertiary hydroxyl group is conducive to the addition of a molecule of bromine to the multiple bond [1].

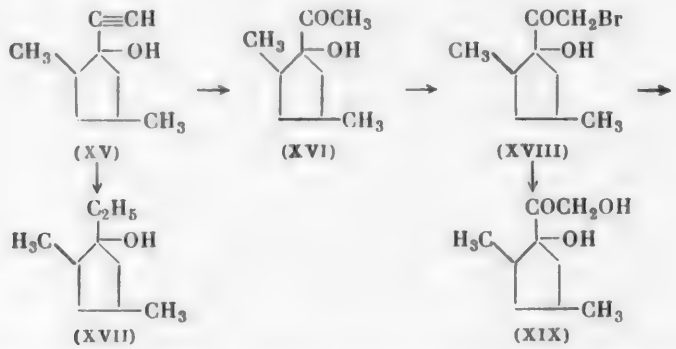
The action of bromine in anhydrous ether on the acetate (XIIIa) formed a crystalline product with m.p. 105° (decomp.), which was apparently the unstable dibromide (XIVa), and which gradually decomposed at room temperature with the liberation of bromine.



(XIIIa) (XIV) (XIVa)

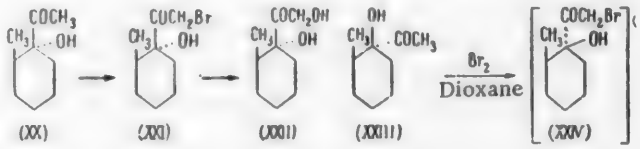
Hydration of 3,5-dimethyl-1-ethynylcyclopentanol (XV), synthesized from 3,5-dimethylcyclopentanone by the Favorskii reaction, gave a high yield of 3,5-dimethyl-1-acetylcyclopentanol (XVI). Exhaustive hydrogenation of the acetylene alcohol (XV) over platinum oxide formed 1-ethyl-3,5-dimethylcyclopentanol (XVII) in high yield.

Bromination of the α-ketol (XVI) with dioxane dibromide gave a low yield of 3,5-dimethyl-1-bromoacetylcyclopentanol (XVIII), whose hydrolysis with an aqueous solution of potassium hydroxide in chloroform formed 3,5-dimethyl-1-hydroxyacetylcyclopentanol (XIX) of unknown configuration.

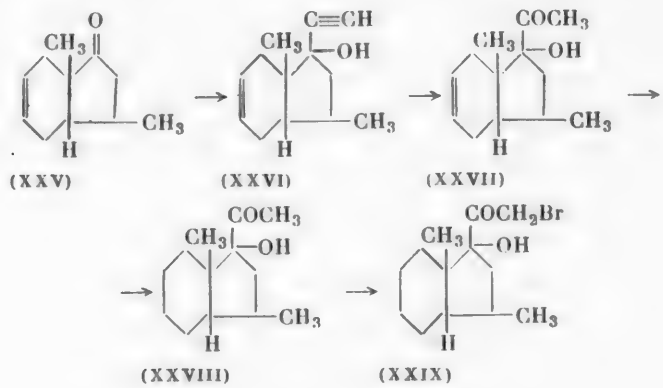


Bromination of cis-2-methyl-1-acetylcyclohexanol (XX) [10] (m.p. 38°) with dioxane dibromide in dioxane yielded crystalline 2-methyl-1-bromoacetylcyclohexanol (XXI) [2]. Hydrolysis of the latter with potassium hydroxide in methanol formed crystalline 2-methyl-1-hydroxyacetylcyclohexanol (XXII) [2].

Under these conditions, the liquid trans-2-methyl-1-acetylcyclohexanol (XXIII) [10] gave liquid trans-2-methyl-1-bromoacetylcyclohexanol (XXIV), which could not be isolated in a pure form.



Ethynylation of 3,8-dimethyl-Δ^5-tetrahydroindanone (XXV) [8] with sodium acetylide in liquid ammonia formed 3,8-dimethyl-1-ethynyl-Δ^5-tetrahydroindanol (XXVI) [8], whose hydration gave crystalline 3,8-dimethyl-1-acetyl-Δ^5-tetrahydroindanol (XXVII) of unknown configuration. Catalytic hydrogenation over platinum oxide converted the latter to 3,8-dimethyl-1-acetylhexahydroindanol (XXVIII). Bromination of the α-ketol (XXVIII) with bromine in dioxane yield 3,8-dimethyl-1-bromoacetylhexahydroindanol (XXIX), but after hydrolysis of the latter it was not possible to isolate the ketodiol corresponding to it.



EXPERIMENTAL

The starting dimethylethynylcarbinol (I) was prepared by the Favorskii reaction as described previously [5]. Dimethylacetylcarbinol (II) and its acetate (V) were synthesized by the procedure described by I.N. Nazarov [6]. The bromooxide (XIII) (b.p. 78-78.5° at 2 mm, $n^{20}D$ 1.5040) was synthesized by the procedure described in the first communication of this series [1]. 3,5-Dimethylcyclopentanone (b.p. 152-153.5°, $n^{20}D$ 1.4332) was prepared by the cyclohydration of vinylisopropenylacetylene in the presence of HCl with subsequent catalytic hydrogenation of the cyclopentenone formed.

Cis- and trans-2-methyl-1-acetylcyclohexanols (XX and XXIII) were prepared by hydration of the acetylene alcohols by the procedure described previously [10]. 3,8-Dimethyl-Δ^5-tetrahydroindanone (b.p. 92-95° at 8 mm, $n^{20}D$ 1.4880) was prepared by diene synthesis from butadiene and 1,3-dimethyl-Δ^1-cyclopentenone-5 as described previously [8]. Dioxane dibromide (m.p. 66°) was prepared by mixing bromine and dioxane as described previously [9].

Preparation of dimethylbromoacetylcarbinol (III). Over a period of 25 minutes, 50 g of dioxane dibromide was added portionwise to a solution of 20 g of dimethylacetylcarbinol (II) in 160 ml of dioxane. After 30 minutes, the dioxane was removed in vacuum at a bath temperature of 40-50° and the residue vacuum distilled. We obtained 21.6 g (60%) of dimethylbromoacetylcarbinol (III) [6] as a colorless liquid with a lacrimatory action and b.p. 106-109° (12 mm), $n^{20}D$ 1.4850.

Preparation of dimethylhydroxyacetylcarbinol (IV). 25 ml of a 10% solution of potassium hydroxide in methanol was added to a solution of 6 g of dimethylbromoacetylcarbinol (III) in 5 ml of methanol. The precipitate of potassium bromide (3.5 g), which precipitated immediately, was filtered off, the methanol removed under reduced pressure and the residue extracted with ether and distilled.

We obtained 2.7 g (68.5%) of dimethylhydroxyacetylcarbinol [6] as a colorless, immobile liquid with b.p. 73.5° (1.5 mm), $n^{20}D$ 1.4496.

Found %: C 49.98, 49.86; H 9.21, 9.11. $C_5H_{10}O_3$. Calculated %: C 50.08; H 8.50.

Preparation of acetate of dimethylbromoacetylcarbinol (VI). Over a period of 15 minutes, 35 g of dioxane dibromide was added in small portions to a solution of 30 g of the acetate of dimethylacetylcarbinol (V) [6] in 100 ml of anhydrous ether. The ether was then distilled off under slightly reduced pressure and the residue vacuum distilled. We obtained 19 g (61%) of the acetate of dimethylbromoacetylcarbinol (VI) as a liquid with b.p. 106.5-109.5° (12 mm), $n^{20}D$ 1.4695, and with a sharp, lacrimatory smell. On standing, the carbinol (VI) changed into crystals with m.p. 43-44°.

Preparation of diacetate of dimethylhydroxyacetylcarbinol (VII). A solution of 5.1 g of potassium acetate in 30 ml of anhydrous methanol was added to a solution of 10.5 g of the acetate of dimethylbromoacetylcarbinol (VI) in 20 ml of anhydrous methanol and the mixture boiled under reflux for ten hours. When the mixture had been cooled, the precipitate of potassium bromide (4 g) was filtered off, the methanol removed in vacuum, and the residue extracted with anhydrous ether. Vacuum distillation yielded 6 g (70%) of the diacetate of dimethylhydroxyacetylcarbinol as a colorless, mobile liquid with b.p. 96-96.5° (2 mm), $n^{20}D$ 1.4370.

Found %: C 53.06, 53.20; H 6.96, 7.00. $C_9H_{14}O_5$. Calculated %: C 53.43; H 6.99.

Preparation of 1-acetylcyclohexanol (IXa). Into a three-necked flask, fitted with a mechanical stirrer, a reflux condenser, and a thermometer, was placed 1 liter of methanol, 160 ml of water, 66 ml of concentrated sulfuric acid, 40 g of mercuric sulfate, and 200 g of 1-ethynylcyclohexanol (VIII) and the mixture heated on a water bath at 60°. After ten-minutes heating, the temperature of the reaction mixture rose to 70° and, simultaneously, a voluminous milk-white precipitate of a mercury compound formed. The temperature of the reaction was prevented from rising above 65-70° by ice cooling. After the thermal effect, the mixture was heated at 60° for a further one hour. The precipitate was then filtered off, the methanol removed under reduced pressure and ether and 50 ml of water added to the residue, which was neutralized with sodium bicarbonate. The ether layer was dried with sodium sulfate and the residue after removal of the ether was vacuum distilled. We obtained 180 g (78.5%) of 1-acetylcyclohexanol (IXa) [2, 3] as a mobile, colorless liquid with b.p. 92-94° (15 mm), $n^{20}D$ 1.4675.

The semicarbazone had m.p. 197-197.5° (from alcohol) and the 2,4-dinitrophenylhydrazone melted at 203-204.5°.

Preparation of the acetate of 1-acetylcyclohexanol (IXb). Into a three-necked, round-bottomed flask, fitted with a mechanical stirrer, a thermometer and a dropping funnel, was placed 120 g of acetic anhydride, containing 3-4 drops of concentrated sulfuric acid. Then 80 g of 1-acetylcyclohexanol (IXa) was added from a dropping funnel with cooling in ice and the temperature of the reaction mixture was kept below 40-45°. When the α-ketol (IXa) had been added, the mixture was left at room temperature overnight. On the following day, the reaction mixture was stirred for two hours at 70°, then diluted with water (25 ml) and ether, and neutralized with sodium carbonate, and the product extracted with ether and dried with sodium sulfate. Vacuum distillation yielded 95 g (92%) of the acetate of 1-acetylcyclohexanol as a mobile, colorless liquid with b.p. 85-86° (2 mm), $n^{20}D$ 1.4605.

Found %: C 65.43, 65.40; H 8.74, 8.90. $C_{10}H_{16}O_3$. Calculated %: C 65.22; H 8.70.

The 2,4-dinitrophenylhydrazone melted at 155.5-156.5° (from alcohol) and did not depress the melting point of another sample prepared in our laboratory by another method [1].

Acetylation of the α-ketol (IXa) in pyridine did not proceed smoothly and formed a mixture of products which had an extended boiling range.

Preparation of 1-bromoacetylcyclohexanol (Xa). a) 110 g of dioxane dibromide was added in small portions over 20 minutes to a solution of 60 g of α-ketol (IXa) in 550 ml of dioxane. The dioxane was then removed in vacuum at a water-bath temperature of 45-50° and the residue vacuum distilled. We obtained 65 g (69.60%) of 1-bromoacetylcyclohexanol as an immobile, light-yellow liquid with b.p. 113.5-114.5° (1 mm), $n^{20}D$ 1.5190.

Found %: C 43.39, 43.45; H 5.90, 5.96; Br 36.25, 36.03. $C_8H_{13}O_2Br$. Calculated %: C 43.44; H 5.88; Br 36.15.

The crystalline isomer of bromoacetylhexanol (Xa) was not isolated.

b) 35 g of dioxane dibromide was added over eight minutes to a solution of 20 g of α-ketol (IXa) in 40 ml of anhydrous ether. The solvent was then removed in vacuum and the oily residue dissolved in 100 ml of 60% ethanol. When cooled to −5°, the solution deposited crystals of a bromide of unknown structure (11 g) with m.p. 118-118.5° (from alcohol).

Found %: Br 36.14, 36.25. $C_8H_{13}O_2Br$. Calculated %: Br 36.15.

After removal of the crystals, the filtrate was evaporated in vacuum. The residue was dissolved in ether, dried with sodium sulfate and vacuum distilled. We obtained 10.5 g (34%) of 1-bromoacetylcyclohexanol (Xa) as a viscous liquid with b.p. 118.5-119° (2 mm) and $n^{20}D$ 1.5120, and which darkened in air.

c) Bromination of 14.2 g of α-ketol (IXa) with bromine in chloroform yielded 9 g of the isomeric crystalline bromide with m.p. 118-118.5° and only 1.2 g of the liquid bromoketol (Xa). Together with this, we isolated 5 g of high-boiling products, which were apparently compounds of higher degrees of bromination.

Preparation of 1-acetoxy-1-bromoacetylcyclohexanol (Xb). 27 g of dioxane dibromide was added in small portions over a period of 5-7 minutes to a solution of 20 g of the acetate of 1-acetylcyclohexanol (IXb) in 40 ml of anhydrous ether. The ether and the dioxane were removed in vacuum and the residue distilled. We obtained 15 g (52%) of the acetate of 1-bromoacetylcyclohexanol as a viscous, yellow liquid with b.p. 126-127.5° (3 mm) and $n^{20}D$ 1.5000. On prolonged standing, it gradually crystallized as platelets with m.p. 34-35° (from pentane).

Found %: C 45.38, 45.32; H 5.80, 5.74. $C_{10}H_{15}O_3Br$. Calculated %: C 45.60; H 5.70.

Preparation of the acetate of bromohydrin (XIV). a) A solution of 10 g of the bromooxide (XIII) (b.p. 78-78.5° at 2 mm, $n^{20}D$ 1.5040) in 100 ml of glacial acetic acid was heated for one hour on a boiling-water bath (liquid temperature 95°) and for two hours at 65-75°. When the reaction mixture was heated at above 100°, tar formation was observed. The clear, light-yellow solution was diluted three-fold with water, neutralized with sodium bicarbonate, extracted with ether, the ether extract dried with sodium sulfate, and the ether evaporated. We obtained 11.5 g of a thick, clear liquid, which yielded, on treatment with 40 ml of petroleum ether, 1 g of the known bromohydrin acetate (XIV) as silvery-white plates with m.p. 96-97° (from petroleum ether + n-hexene), undepressed by admixture with an authentic sample.

b) Over a period of five minutes, 3 ml of bromine was added with cooling with cold water to a mixture of 8.5 g of the acetate of 1-vinylcyclohexanol (XIIIa) (b.p. 83° at 13 mm, $n^{20}D$ 1.4590), 45 ml of dioxane and 25 ml of water (the acetate did not dissolve completely). After ten minutes, crystals were deposited and these were filtered off, washed with water on the filter and dried. We obtained 11.5 g (84.5%) of the bromohydrin acetate (XIV) as colorless crystals with m.p. 96-97° (from petroleum ether), undepressed by admixture with an authentic sample [1]. In addition, the filtrate yielded about 1 g of an oil, which was heavier than water and which was not examined further.

Oxidation of the bromohydrin acetate (XIV) with chromium trioxide in acetic acid gave a good yield of 1-acetoxy-1-bromoacetylcyclohexanol (Xb) described above.

c) With cooling, 2.6 ml of bromine was added to a solution of 8.4 g of the acetate of 1-vinylcyclohexanol (XIIIa) in 100 ml of anhydrous ether. A yellow, crystalline product precipitated. The crystals were filtered off and washed with ether on the filter. We obtained 5 g of crystals with m.p. 105° (decomp.). When the latter were stored in a bottle with a ground-glass stopper at room temperature, the product decomposed. The crystals were converted into a liquid product consisting of two layers, the upper one colorless and the lower one a heavy, brown oil with a bromine smell. The reaction was acid.

Preparation of 1-hydroxyacetylcyclohexanol (XI). A solution of 15 g of potassium hydroxide in 150 ml of water was added in small portions, over a period of 40 minutes, to a solution of 58 g of α-bromoketol (Xa) (b.p. 113-115° at 1 mm, $n^{20}D$ 1.5172) in 600 ml of chloroform in the presence of phenolphthalein with shaking in a separating funnel. Each successive portion of alkali was added only when the solution was decolorized. At the end, the solution had a weakly alkaline reaction. 0.3 ml of 50% acetic acid was added to neutralize the solution, which was decolorized. The chloroform layer was separated and the aqueous layer extracted with chloroform. The combined chloroform extracts were dried with sodium sulfate and the chloroform removed in vacuum. The residue of about 40 g crystallized on cooling. The crystals were separated and recrystallized from petroleum ether. We obtained 26.4 g (63%) of 1-hydroxyacetylcyclohexanol (XI) as colorless crystals with m.p. 86-87.5°.

The 2,4-dinitrophenylhydrazone formed crystals with m.p. 152-154° (from alcohol).

Found %: N 16.19, 16.05. $C_{14}H_{18}O_6N_4$. Calculated %: N 16.56.

Under these conditions, the acetate of 1-bromoacetylcyclohexanol (Xb) gave liquid, uncrystallizable hydrolysis products, containing bromine.

An attempt to prepare the diacetate of 1-hydroxyacetylcyclohexanol (XII) by acetolysis of the acetate of 1-bromoacetylcyclohexanol (Xb) was unsuccessful. It yielded liquid products containing bromine.

Preparation of 3,5-dimethyl-1-ethynylcyclopentanol (XV). Into a round-bottomed flask, fitted with a mechanical stirrer, a thermometer and a dropping funnel, was placed 120 g of powdered potassium hydroxide and 300 ml of anhydrous ether and the mixture saturated for 1.5 hours at 0° with acetylene. Then, over a period of 2.5 hours, with cooling to −3 to −5°, a solution of 80 g of dimethylcyclopentanone (b.p. 152-153.5°, $n^{20}D$ 1.4332) in 80 ml of anhydrous ether was added to the mixture from the dropping funnel and the mixture stirred for a further two hours at 0° and left overnight in an ice bath. On the following day, the ether layer was separated, the aqueous layer extracted with ether, and the combined ether extracts treated with 5% hydrochloric acid and water, and dried with sodium sulfate. Vacuum distillation yielded 50 g of 3,5-dimethyl-1-ethynylcyclopentanol (XV) as a colorless liquid with b.p. 82-84° (20 mm), $n^{20}D$ 1.4620.

Found %: C 77.82, 77.68; H 10.49, 10.42. $C_9H_{14}O$. Calculated %: C 78.20; H 10.21.

Preparation of 3,5-dimethyl-1-ethylcyclopentanol (XVII). A solution of 3 g of 3,5-dimethyl-1-ethynylcyclopentanol (XV) in 10 ml of methanol was hydrogenated in the presence of platinum oxide, when 1100 ml of hydrogen was absorbed while the calculated amount was 1040 ml. Vacuum distillation yielded 2.6 g of 3,5-dimethyl-1-ethylcyclopentanol as a mobile, colorless liquid with b.p. 81-82° (18 mm), $n^{20}D$ 1.4538.

Found %: C 75.40, 75.62; H 12.76, 12.53. $C_9H_{18}O$. Calculated %: C 75.97; H 12.60.

Preparation of 3,5-dimethyl-1-acetylcyclopentanol (XVI). 14.5 g of 3,5-dimethyl-1-ethynylcyclopentanol (XV) was added to 70 ml of methanol containing 11 ml of water, 4.8 g of concentrated sulfuric acid, and 3 g of mercuric sulfate and the mixture stirred at 60° for two hours. Then the methanol was removed under reduced pressure (bath temperature 35-40°), the residue diluted with ether and water, and neutralized with sodium bicar-

bonate and the product dried with sodium sulfate and vacuum distilled. We obtained 11 g of 3,5-dimethyl-1-acetylcyclopentanol as a colorless liquid with b.p. 98-100° (14 mm), $n^{20}D$ 1.4590.

Found %: C 68.86, 68.99; H 10.68, 10.60. $C_9H_{16}O_2$. Calculated %: C 69.10; H 10.20.

Preparation of 3,5-dimethyl-1-bromoacetylcyclopentanol (XVIII). Over a period of 10 minutes, 8 g of dioxane dibromide was added to a solution of 5 g of α-ketol (XVI) in 20 ml of dioxane. The mixture was then diluted with water, neutralized with sodium bicarbonate and extracted with ether and the product dried with sodium sulfate and vacuum distilled. We obtained 2.3 g of 3,5-dimethyl-1-bromoacetylcyclopentanol as a heavy liquid, which fumed and rapidly darkened in air and which could not be purified.

Preparation of 3,5-dimethyl-1-hydroxyacetylcyclopentanol (XIX). 6 ml of 10% aqueous potassium hydroxide solution was added in small portions with shaking in a separating funnel to a solution of 2.3 g of crude bromoketol (XVIII), prepared in the previous experiment, in 10 ml of chloroform in the presence of phenolphthalein. The chloroform was separated, the aqueous layer extracted with chloroform and the combined chloroform solutions dried with sodium sulfate. Removal of the solvent in vacuum at a bath temperature of 45° left a residue of 1.9 g of oil ($n^{20}D$ 1.4962), which partly crystallized on standing and was apparently impure 3,5-dimethyl-1-hydroxyacetylcyclopentanol.

The 2,4-dinitrophenylhydrazone formed crystals with m.p. 198-200° (from aqueous alcohol).

Found %: N 17.08, 17.18. $C_{15}H_{20}O_6N_4$. Calculated %: N 17.77.

Preparation of cis-2-methyl-1-bromoacetylcyclohexanol (XXI). 14.5 g of dioxane dibromide was added in small portions to a solution of 9 g of cis-α-ketol (XX) (m.p. 37-38°) in 45 ml of dioxane at 25°. The solution was completely decolorized after five minutes. The dioxane was removed in vacuum at a bath temperature of 60° and the residue distilled. We obtained 9 g (67%) of cis-2-methyl-1-bromoacetylcyclohexanol as a liquid; it had m.p. 68-68.5° (from n-hexane), b.p. 109-113° (1.5 mm), $n^{20}D$ 1.5062.

Found %: C 46.33, 46.15; H 6.64, 6.78; Br 34.53. $C_9H_{15}O_2Br$. Calculated %: C 45.95; H 6.43; Br 34.0.

Preparation of trans-2-methyl-1-bromoacetylcyclohexanol (XXIV). 25 g of dioxane dibromide was added in portions to a solution of 15 g of trans-α-ketol (XXIII) (b.p. 82-83° at 9 mm, $n^{20}D$ 1.4610) in 60 ml of dioxane. Ten minutes after the solution had been decolorized, the dioxane was removed in vacuum at a bath temperature of 50-55° and the residue vacuum distilled. After the first distillation, we obtained about 15 g of a crude product, which boiled over a wide range (b.p. 110-122° at 1.5 mm, $n^{20}D$ 1.5110-1.5155). After three vacuum distillations, we isolated 2.2 g of trans-2-methyl-1-bromoacetylcyclohexanol as a colorless liquid with b.p. 119.5-120° (2.5 mm) $n^{20}D$ 1.5132, with a high bromine content and a low carbon content.

Found %: C 44.80, 44.77; H 6.15, 6.14; Br 35.88, 35.08. $C_9H_{15}O_2Br$. Calculated %: C 45.95; H 6.43; Br 34.00.

Preparation of cis-2-methyl-1-hydroxyacetylcyclohexanol (XXII). 3 g of cis-α-bromoketol (XXI) (m.p. 68-68.5°) was added to 8 ml of a 10% solution of potassium hydroxide in methanol, the potassium bromide precipitate filtered off, the filtrate evaporated to dryness in vacuum and the residue extracted with ether. After removal of the ether in vacuum, the residue partially crystallized. We obtained 0.25 g of cis-2-methyl-1-hydroxyacetylcyclohexanol [2] as colorless crystals with m.p. 76-77.5° (from petroleum ether).

The thiosemicarbazone had m.p. 208-209.5° (from methanol).

Synthesis of 3,8-dimethyl-1-ethynyl-Δ^5-tetrahydroindanol (XXVI). Into a three-necked, round-bottomed flask, fitted with a mechanical stirrer, a thermometer and a dropping funnel, was placed a solution of 9.2 g of sodium in 350 ml of liquid ammonia and acetylene passed through for three hours at −73 to −76°. Then, over a period of one hour, a solution of 35 g of dimethyltetrahydroindanone (XXV) in 75 ml of anhydrous ether was added dropwise. The mixture was stirred in a stream of acetylene for a further 45 minutes and then left overnight in a bath of solid carbon dioxide. On the following day the mixture was stirred at room temperature until the ammonia had almost completely disappeared, the residue diluted with 100 ml of anhydrous ether and 50 g of ammonium chloride added. After complete evaporation of the ammonia, 150 ml of water was added, the ether layer separated, the aqueous layer extracted with ether and the combined ether extracts dried with sodium sulfate and vacuum distilled. We obtained 35 g (86%) of 3,8-dimethyl-1-ethynyl-Δ^5-tetrahydroindanol as a colorless liquid with b.p. 92-95° (3 mm), $n^{20}D$ 1.5045. The configuration was not established.

Preparation of 3,8-dimethyl-1-acetyl-Δ^5-tetrahydroindanol (XXVII). 1.8 g of 3,8-dimethyl-1-ethynyl-Δ^5-tetrahydroindanol (XXV) was hydrated with a mixture of 0.25 g of mercuric sulfate, 0.4 ml of concentrated sulfuric acid, 6 ml of methanol and 1 ml of water for 2.5 hours at 60° with stirring. The mixture was then diluted with water and ether, neutralized with sodium bicarbonate, the ether layer separated, the aqueous layer extracted with ether and the product dried with sodium sulfate and vacuum distilled. We obtained 1.3 g of a substance with b.p. 123-128° (4.5 mm), forming a mixture of crystals and liquid (apparently a mixture of isomers) from which we isolated 0.8 g (40%) of 3,8-dimethyl-1-acetyl-Δ^5-tetrahydroindanol as colorless crystals with m.p. 91-92° (from ether).

Found %: C 74.63, 74.96; H 9.73, 9.85. $C_{13}H_{20}O_2$. Calculated %: C 74.94; H 9.70.

The configuration of the α-ketol at the two asymmetric centers (C-1 and C-3) was not established.

Preparation of 3,8-dimethyl-1-acetylhexahydroindanol (XXVIII). A solution of 4.2 g of α-ketol (XXVII) in 25 ml of ethanol was hydrogenated in the presence of platinum oxide. After 45 minutes, 442 ml of hydrogen (430 ml of hydrogen was required, according to calculation) had been absorbed. After removal of the ethanol, we obtained 4 g of colorless crystals of 3,8-dimethyl-1-acetyltetrahydroindanol with m.p. 114-114.5° (from petroleum ether).

Found %: C 73.69, 73.72; H 10.45, 10.48. $C_{13}H_{22}O_2$. Calculated %: C 74.20; H 10.55.

Preparation of 3,8-dimethyl-1-bromoacetylhexahydroindanol (XXIX). Over a period of twelve minutes, 2.4 g of dioxane dibromide was added in small portions to a solution of 2 g of α-ketol (XXVIII) (m.p. 113.5-114°) in 15 ml of dioxane. The dioxane was then removed in vacuum at a bath temperature of 45° and the partially crystalline residue yielded 1.5 g of 3,8-dimethyl-1-bromoacetylhexahydroindanol as colorless crystals with m.p. 111-112.5° (from petroleum ether).

Found %: C 53.86, 53.95; H 7.27, 7.21; Br 27.99, 27.55. $C_{13}H_{21}O_2Br$. Calculated %: C 53.96; H 7.26; Br 27.70.

An attempt to hydrolyze the α-bromoketol (XXIX) into 3,8-dimethyl-1-hydroxyacetylhexahydroindanol was unsuccessful. When chloroform or ether solutions of the α-bromoketol were treated with an aqueous solution of potassium hydroxide, the original α-bromoketol was recovered unchanged. When the α-bromoketol was treated with a methanol solution of potassium hydroxide, a small precipitate of potassium bromide was produced and an oily, uncrystallizable product was formed.

SUMMARY

1. On the examples of dimethylethynylcarbinol, 1-ethynylcyclohexanol, 3,5-dimethyl-1-ethynylcyclopentanol, cis-2-methyl-1-ethynylcyclohexanol and 3,8-dimethyl-1-ethynyl-Δ^5-tetrahydroindanol, a synthesis is described for compounds containing a dihydroxyacetone side chain, characteristic of adrenocortical hormones.

2. The given compounds were obtained by hydration of acetylene alcohols with subsequent bromination and hydrolysis of the α-bromoketols thus formed.

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SYNTHESES OF ANALOGS OF GERANYLACETONE AND PSEUDOIONONE

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Analogs of geranylacetone and pseudoionone are the starting materials for the synthesis of the corresponding analogs of the important natural isoprenoid compounds, vitamin A, carotene, farnesol and also phytol, a component part of vitamins K and E.

Recently we reported three different methods of synthesizing ketones of the isoprenoid type, developed in laboratory:

1) by the action of sodioacetoacetic ester on halogen derivatives of the allyl type (method A),

2) by the interaction of vinyl- and ethynylcarbinols with acetoacetic ester (method B),

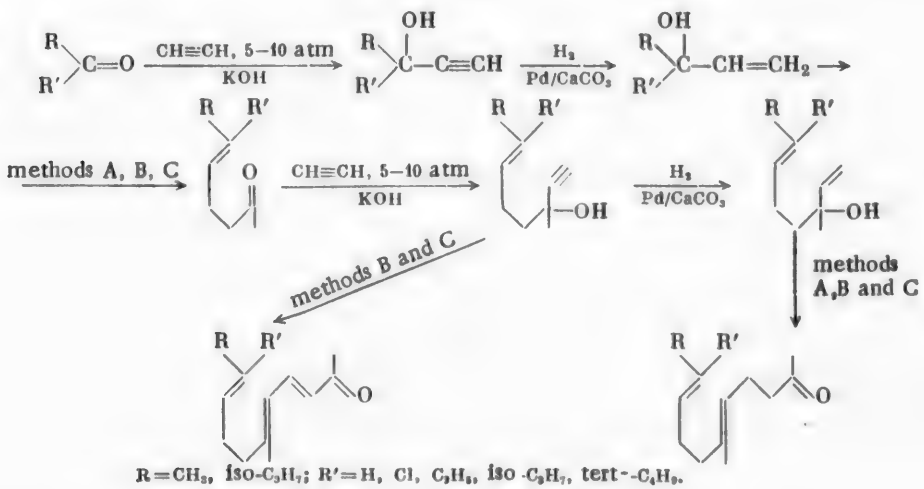
3) by the pyrolysis of acetoacetates of vinyl- and ethynylcarbinols (method C).

By these methods we were able to prepare methylheptenone, methylheptadienone and their analogs [1, 2].

Condensation of methylheptenone and its analogs with acetylene under a pressure of 5-10 atmos gave an almost quantitative yield of dehydrolinalool and its analogs. The latter were partially hydrogenated over a Pd-catalyst to yield linalool and its analogs [3].

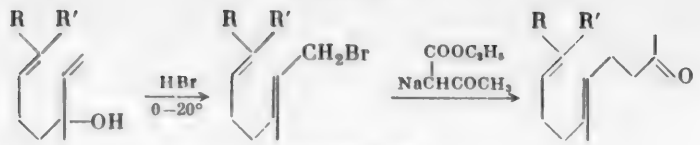
We used the methods (A-C) of synthesizing isoprenoid ketones, which we studied, for the synthesis of various analogs of geranylacetone and also analogs of pseudoionone (by methods B and C) (the synthesis of geranylacetone, pseudoionone and pseudoirone was reported separately [4] (see scheme).

Scheme

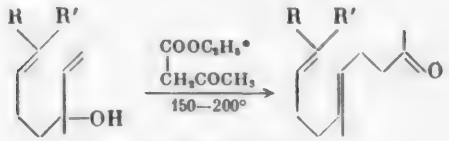


R=CH₃, iso-C₃H₇; R′=H, Cl, C₂H₅, iso-C₃H₇, tert-C₄H₉.

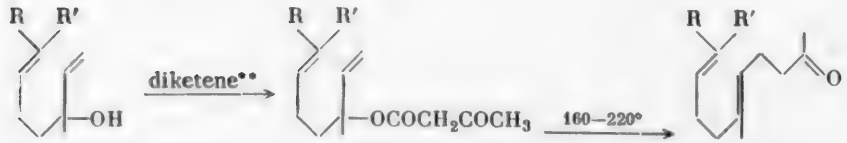
Method A



Method B



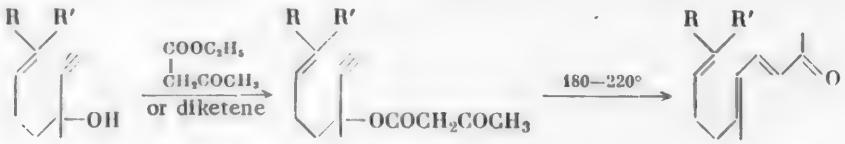
Method C



The analogs of geranylacetone synthesized by the methods described above are presented in Table 2.

The synthesis of pseudoionone analogs was studied by means of methods B and C.

We obtained pseudoionone analogs by heating dehydrolinalool analogs with acetoacetic ester, as in the pyrolysis of acetoacetates of dehydrolinalool analogs, synthesized by means of diketene (Table 3).



The yield of the bulk of the pseudoionones, obtained by the two methods, was 50-70%, with the exception of the chlorine analog (XVI), which was obtained in 12-24% yield, due to its instability on heating.

As was also established previously [4, 7], the pyrolysis of acetoacetates of dehydrolinalools shows stereochemical preference and leads to the formation of mainly one of the isomers of the pseudoionones. The second isomer is present in insignificant amounts (less than 10%) and its isolation therefore presents great difficulties. However, for the isopropyl (XVIII) and the diisopropyl (XX) analogs of pseudoionones, we were able to isolate the two stereoisomeric forms (Table 3) as their dinitrophenylhydrazones.

The analogs of geranylacetone and pseudoionone obtained were characterized by the UV absorption spectra. For all the geranylacetone analogs, the characteristic absorption maxima λ_{max} (in isooctane), was at about 278 mμ (Table 2).

The spectral curves of the 2,4-dinitrophenylhydrazones of all the pseudoionone analogs obtained had the same absorption maximum values, which agreed with the absorption maximum of the 2,4-dinitrophenylhydrazone of natural pseudoionone (Table 3). This indicates that the structures of the pseudoionone analogs obtained are identical with natural pseudoionone.

EXPERIMENTAL

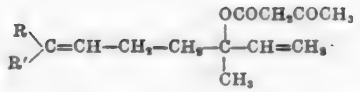
Method A

6-Methylundecadien-2,6-one-10 (VIII). Dry hydrogen bromide was passed into 507 g of 6-methyloctadien-2,7-ol-6, cooled in a mixture of ice and salt, until the weight had increased by 305 g and then the reaction

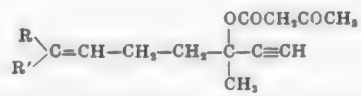
•Linalool [4, 5] and its analogs were reacted with acetoacetic ester without catalysts.

••The action of diketene on linalool [4, 6] and its analogs in the presence of small amounts of triethylamine or piperidine formed the corresponding acetoacetates (Table 1).

TABLE 1



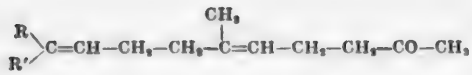
Sample No.	R	R′	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR* found	MR* calc.	Found, % C	Found, % H	Calculated, % C	Calculated, % H	Yield (in %)
(I)	CH_3	Cl	130—132° (1)	1.4781	1.0557	69.32	67.83	60.18, 60.27	7.71, 7.88	60.35	7.35	56.5
(II)	CH_3	C_2H_5	106—107 (0.2)	1.4650	0.9645	72.31	72.20	71.67, 71.62	9.44, 9.45	71.39	9.58	79.3
(III)	CH_3	tert-C_4H_9	115—117 (0.02)	1.4685	0.9572	81.39	81.39	72.99, 73.10	10.27, 10.24	72.86	10.00	87.0



(IV)	CH_3	H	86—87° (0.05)	1.4657	0.98935	62.11	61.37	70.35, 70.35	8.33, 8.20	70.27	8.10	81
(V)	CH_3	Cl	112 (0.07)	1.4802	1.0899	66.92	66.23	60.22, 60.32	6.78, 6.76	60.81	6.62	82
(VI)	CH_3	C_2H_5	112—113 (0.2)	1.4705	0.9641	70.86	70.67	72.23, 72.26	9.00, 8.85	71.97	8.84	79
(VII)	CH_3	tert-C_4H_9	117—120 (0.02)	1.4738	0.9614	81.21	79.80	73.59, 73.66	9.13, 9.16	73.38	9.35	81

*MR was calculated everywhere for the ketonic forms.

TABLE 2



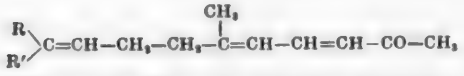
Sample No.	R	R′	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR found	MR calc.	Yield (in %) of method A	B	C
(VIII)	CH_3	H	114—118° (12)	1.4619	0.8767	56.43	56.69	72.8	—	—
(IX)	CH_3	Cl	87—90 (0.5)	1.4795	0.9846	61.83	61.56	75.8	56	48
(X)	CH_3	C_2H_5	106 (1.5)	1.4670	0.8766	65.93	65.92	57	59.5	60
(XI)	CH_3	iso-C_3H_7	108 (1.5)	1.4689	0.8775	70.55	70.57	61	55	—
(XII)	CH_3	tert-C_4H_9	120—126 (4)	1.4710	0.8700	75.68	75.16	67	62	62.6
(XIII)	iso-C_3H_7	iso-C_3H_7	117—118 (2.5)	1.4681	0.8266	80.46	79.80	68	56.6	54.6

•Data refer to 2,4-dinitrophenylhydrazone (2,4-DNPH).

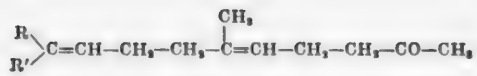
••Data refer to semicarbazone (SC).

•••In n-heptane.

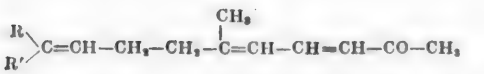
TABLE 3



Sample No.	R	R′	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR found	MR calc.	Yield (in %) of method B	C
(XIV)	CH_3	CH_3	89—90° (0.1)	1.5285	—	—	—	55	50
(XV)	CH_3	H	78—90 (0.03)	1.5280	0.9132	59.69	56.22	40.2	30.2
(XVI)	CH_3	Cl	118—119 (2)	1.5390	1.0099	65.74	61.09	24.4	12.3
(XVII)	CH_3	C_2H_5	127—130 (2)	1.5257	0.9141	69.24	65.46	49	59
(XVIII)	CH_3	iso-C_3H_7	135—138 (2)	1.5183	0.9082	73.56	70.08	52	—
(XIX)	CH_3	tert-C_4H_9	128—134 (3)	1.5205	0.8930	79.72	74.69	71.6	69
(XX)	iso-C_3H_7	iso-C_3H_7	128—130 (1)	1.5145	0.8887	84.39	79.31	65	40



Found (%)		Calculated (%)		λ_{max}	lg ε	2,4-DNPH or SC		
C	H	C	H	in iso-octane		melting point	found	calc.
79.73, 79.80	11.03, 10,85	80.00	11.11	280***	1.430	29—30*	15.51, 15.89	15.55
67.32, 67.28	8.84, 8.68	67.13	8.86	278	2.038	103—105**	15.76, 15.77	15.47
80.63, 80.78	11.36, 11.36	80.72	11.61	281	1.55	76—77**	15.79, 15.88	15.82
81.17, 80.86	12.02, 11.71	81.02	11.79	278	1.607	80—81**	15.30, 15.04	15.05
81.28, 81.68	11.94, 12.08	81.35	11.86	275	1.760	121.5—123**	14.72, 14.52	14.34
81.18, 81.49	12.18, 12.41	81.53	12.07	278	1.64	77—78*	12.99	13.01
						117—118**	13.37, 13.39	13.67



Found (%)		Calculated (%)		2,4-DNPH		
C	H	C	H	melting point	λ_{max} (alcohol)	lg ε
80.97, 80.99	10.30, 10.49	81.19	10.49	117—118°	228, 268, 307, 397	4.090, 4.091, 4.150, 4.430
				147—148	228, 268, 306, 400	4.238, 4.228, 4.298, 4.500
80.92, 80.60	9.87, 10.11	80.89	10.11	122—124	224, 271, 307, 398	4.201, 4.277, 4.355, 4.573
68.00, 67.91	7.72, 7.77	67.76	8.00	158—161	224, 271, 307, 398	4.201, 4.277, 4.355, 4.573
81.42, 81.70	10.49, 10.33	81.50	10.75	114—115	228, 269, 307, 398	3.985, 3.859, 4.036, 4.280
82.04, 81.89	10.95, 11.10	81.73	10.98	94—95	228, 268, 306, 397	4.174, 4.203, 4.234, 4.507
				119—120	226, 269, 306, 398	4.138, 4.138, 4.218, 4.416
82.29, 82.27	11.19, 11.20	82.05	11.12	115—117	235, 266, 307, 398	4.228, 4.198, 4.254, 4.514
82.15, 82.43	11.52, 11.36	82.15	11.36	156—157	228, 269, 306, 398	4.184, 4.192, 4.270, 4.513
				125—126	228, 268, 305, 398	4.000, 4.014, 4.069, 4.332

mixture was left for a day at room temperature. The 8-bromo-6-methyloctadiene-2,6 (an analog of geranyl bromide) obtained was separated from the water, washed with 5% sodium bicarbonate solution and water, dried over sodium sulfate and used for the condensation with sodioacetoacetic ester without preliminary distillation.

To sodium methylate, prepared from 1100 ml of methyl alcohol and 93.6 g of metallic sodium, was added 673 g of acetoacetic ester at room temperature with stirring and the reaction mixture was heated at 60° for 30 minutes. After this, the bromide above was added over a period of one hour to the sodioacetoacetic ester obtained at −10°, and the reaction mixture was stirred at room temperature for three hours. The methyl alcohol was then removed under reduced pressure, a solution of 296 g of sodium hydroxide in 2 liters of water added to the residue and the mixture stirred at 65-70° for six hours. The reaction mixture was made acid to Congoby the addition of concentrated hydrochloric acid with cooling and the product extracted with ether, carefully washed with 5% sodium bicarbonate solution and water, dried over anhydrous sodium sulfate and vacuum distilled. We obtained 475 g (72.8%) of 6-methylundecadien-2,6-one-10 with b.p. 114-118° (12 mm), $n^{20}D$ 1.4619.

2-Chloro-6-methylundecadien-2,6-one-10 (IX). With cooling in snow and salt, a stream of dry hydrogen bromide was passed into a solution of 93.6 g of 2-chloro-6-methyloctadien-2,7-ol-6 in 150 ml of isooctane until the weight had increased by 45 g and the reaction mixture was left overnight at room temperature. The isooctane layer was separated from the water, washed with saturated sodium bicarbonate solution and dried over anhydrous magnesium sulfate. The isooctane solution of the primary bromide obtained was added over a period of 1.5 hours at −5 to 10° to a solution, prepared as in the previous experiment from 13.7 g of metallic sodium, 167 ml of methyl alcohol and 135.6 g of acetoacetic ester. The reaction mixture was left overnight at room temperature. The methanol was evaporated under reduced pressure, 43 g of sodium hydroxide in 280 ml of water added to the residue and the mixture stirred at room temperature for two hours and at 65-70° for 9.5 hours. The reaction mixture was made acid to Congo by the addition of 50% sulfuric acid with cooling. The product was extracted with ether and the ether extract washed with 5% sodium bicarbonate solution, dried with sodium sulfate and vacuum distilled. We obtained 87.9 g (75.8%) of 2-chloro-6-methylundecadien-2,6-one-10 with b.p. 87-90° (0.5 mm), $n^{20}D$ 1.4795.

The semicarbazone had m.p. 103-105° (from methanol) and did not depress the melting point of the semicarbazone of ketone (IX), obtained by method B.

Method B

3,7-Dimethyldodecadien-3,7-one-11 (X). A mixture of 84.1 g of 3,7-dimethylnonadien-3,8-ol-7 and 130 g of acetoacetic ester was heated in a Favorskii flask at 150-195° for four hours until the evolution of carbon dioxide ceased (25 ml of alcohol distilled during this). The reaction product was dissolved in ether, washed with 5% sodium bicarbonate solution three times and with water, and dried with baked magnesium sulfate. Two distillations in vacuum yielded 62.2 g (59.5%) of 3,7-dimethyldodecadien-3,7-one-11 with b.p. 105-106° (15 mm), $n^{20}D$ 1.4670.

The semicarbazone had m.p. 76-77° (from methanol) and did not depress the melting point of the semicarbazone of ketone (X) obtained by methods A and C.

2,3,7-Trimethyldodecadien-3,7-one-11 (XI). A mixture of 18.2 g of 2,3,7-trimethylnonadien-3,8-ol-7 and 26 g of acetoacetic ester was heated at 170-190° for one hour. 2620 ml of carbon dioxide was liberated and 4.6 ml of alcohol distilled off. The reaction product was treated as in the previous experiment. Two vacuum distillations yielded 12.3 g (55%) of 2,3,7-trimethyldodecadien-3,7-one-11 with b.p. 107-108° (1.5 mm), $n^{20}D$ 1.4689.

The semicarbazone had m.p. 80-81° (from methanol), undepressed by admixture with the semicarbazone of the ketone obtained by methods A and C.

Method C

3,7-Dimethyldodecadien-3,7-one-11 (X). The starting acetoacetate of 3,7-dimethylnonadien-3,8-ol-7 (II) was obtained in the following way: to a mixture of 12.6 g of 3,7-dimethylnonadien-3,8-ol-7 and 5 drops of triethylamine at 70° was added 7.8 g of diketene over a period of 30 minutes and then heating was continued for a further two hours. The reaction product was dissolved in ether, washed with 5% sodium bicarbonate solution twice and with water and dried with anhydrous magnesium sulfate. Vacuum distillation yielded 15.0 g (79.5%) of the acetoacetate of 3,7-dimethylnonadien-3,8-ol-7 with b.p. 106-107° (0.2 mm), $n^{20}D$ 1.4650.

12.6 g of the acetoacetate (II) described above was heated at 170-185° for 15 minutes; 1130 ml of carbon dioxide was liberated. The reaction product was dissolved in ether and treated as in previous experiments. We obtained 6.3 g (60%) of 3,7-dimethyldodecadien-3,7-one-11 (X) with b.p. 105-106° (15 mm), $n^{20}D$ 1.4670.

2,2,3,7-Tetramethyldodecadien-3,7-one-11 (XII). Over a period of 25 minutes, 4.5 g of diketene was added to a mixture of 9.8 g of 2,2,3,7-tetramethylnonadien-3,8-ol-7 and three drops of trimethylamine at 70°. Heating was continued for a further two hours. Without preliminary treatment or distillation, the reaction product was pyrolyzed at 180-190° for 1.5 hours. 1150 ml of carbon dioxide was liberated. The reaction mixture was extracted with ether and the extract washed with 5% sodium bicarbonate solution and water, dried with magnesium sulfate and distilled. We obtained 7.5 g (62.6% on the carbinol) of 2,2,3,7-tetramethyldodecadien-3,7-one-11 with b.p. 120-126° (4 mm), $n^{20}D$ 1.4710.

The semicarbazone had m.p. 121.5-123° (from alcohol) and did not depress the melting point of the semicarbazone of this ketone, prepared by methods A and B.

2,7-Dimethyl-3-isopropyldodecadien-3,7-one-11 (XIII). Over a period of 0.5 hours, 2.7 g of diketene was added to a mixture of 5.5 g of 2,7-dimethyl-3-isopropylnonadien-3,8-ol-7 and three drops of triethylamine at 70°. Heating was continued for a further two hours. Without preliminary treatment and distillation, the reaction product was pyrolyzed at 180-200° for 0.5 hours. 580 ml of carbon dioxide was liberated. The usual treatment and distillation yielded 3.5 g (54.6%) of 2,7-dimethyl-3-isopropyldodecadien-3,7-one-11 with b.p. 103-105° (0.4 mm), $n^{20}D$ 1.4680.

The semicarbazone had m.p. 117-118° and did not depress the melting point of the semicarbazone of this ketone, prepared by methods A and B.

Method B

2-Chloro-6-methylundecatrien-2,6,8-one-10 (XVI). A mixture of 17.25 g of 2-chloro-6-methylocten-2-yn-7-ol-6 and 65 g of acetoacetic ester was heated at 160-185° for three hours. During this time 2300 ml of carbon dioxide and 7 ml of alcohol were liberated. The reaction product was dissolved in ether, washed with 5% sodium bicarbonate solution and water, and dried with magnesium sulfate. Two vacuum distillations yielded the following fractions: 1st – 90-98° (2 mm), $n^{20}D$ 1.4793, 0.6 g; 2nd – 112-116° (2 mm), $n^{20}D$ 1.5292, 2.3 g; 3rd – 118-119° (2 mm), $n^{20}D$ 1.5390, 5.2 g.

The third fraction was 2-chloro-6-methylundecatrien-2,6,8-one-10. The yield was 24.4%.

The 2,4-dinitrophenylhydrazone had m.p. 158-161° (from alcohol).

2,3,7-Trimethyldodecatrien-3,7,9-one-11 (XVIII). A mixture of 18 g of 2,3,7-trimethylnonen-3-yn-8-ol-7 and 26 g of acetoacetic ester was heated at 176-198° for 1.5 hours. 2650 ml of carbon dioxide and 5 ml of alcohol were liberated. The reaction product was treated in the usual way. After two vacuum distillations it yielded 11.5 g (52%) of 2,3,7-trimethyldodecatrien-3,7,9-one-11 with b.p. 135-138° (2 mm), $n^{20}D$ 1.5183.

The 2,4-dinitrophenylhydrazone of the isopropyl analog of pseudoionone (XVIII) was prepared in the usual way. After many fractional crystallizations from a mixture of alcohol and acetone, it yielded two stereoisomers, one with m.p. 119-120° (about 95%) and the other with m.p. 94-95° (about 5%).

2,7-Dimethyl-3-isopropyldodecatrien-3,7,9-one-11 (XX). A mixture of 15 g of 2,7-dimethyl-3-isopropylnonen-3-yn-8-ol-7 and 15 g of acetoacetic ester was heated at 190-210° for three hours. 1780 ml of carbon dioxide were liberated and 4.4 ml of alcohol distilled off. The reaction product was treated in the usual way. We obtained 11.7 g (65%) of 2,7-dimethyl-3-isopropyldodecatrien-3,7,9-one-11 with b.p. 128-130° (1 mm), $n^{20}D$ 1.5145.

Found %: C 82.15, 82.43; H 11.52, 11.36. $C_{17}H_{28}O$. Calculated %: C 82.15; H 11.36.

The 2,4-dinitrophenylhydrazone was obtained by mixing an alcohol solution of the ketone with an alcohol-dioxane solution of 2,4-dinitrophenylhydrazine hydrochloride. The m.p. was 114-116°. As a result of fractional crystallization from a mixture of ethyl alcohol and benzene, we isolated 91% of the discrete isomer of the 2,4-dinitrophenylhydrazone with m.p. 156-157° and 9% of the discrete isomer of the 2,4-dinitrophenylhydrazone with m.p. 125-126°.

Method C

6-Methylundecatrien-2,6,8-one-10 (XV). The starting acetoacetate of 6-methylocten-2-yn-7-ol-6 (IV) was prepared in the following way: to a mixture of 13.8 g of 6-methylocten-2-yn-7-ol-6 and eight drops of triethylamine heated to 70° was added 10.5 g of diketene with stirring over a period of one hour, at such a rate that the reaction temperature did not exceed 80°. The reaction mixture was heated for a further four hours until the smell of diketene disappeared. The reaction product was extracted with ether, washed with sodium bicarbonate solution and water, dried with sodium sulfate and vacuum distilled. We obtained 18 g (81%) of the acetoacetate of 6-methylocten-2-yn-7-ol-6 with b.p. 86-87° (0.05 mm), $n^{20}D$ 1.4657.

13.6 g of the acetoacetate of 6-methylocten-2-yn-7-ol-6 (IV) was heated at 180-200° for 45 minutes. 1250 ml of carbon dioxide was liberated. The reaction product was washed with 5% sodium bicarbonate solution and water, and dried with sodium sulfate. Distillation in vacuum yielded 3.3 g (30.2%) of 6-methylundecatrien-2,6,8-one-10 (XV) with b.p. 78-80° (0.03 mm), $n^{20}D$ 1.5280.

3,7-Dimethyldodecatrien-3,7,9-one-11 (XVII). 25 g of the acetoacetate of 3,7-dimethylnonen-3-yn-8-ol-7 (VI) was heated at 170-185° for 25 minutes. 2250 ml of carbon dioxide was liberated. The reaction product was washed with saturated sodium bicarbonate solution and water, and dried with magnesium sulfate. Distillation in vacuum yielded 12.15 g (59%) of 3,7-dimethyldodecatrien-3,7,9-one-11 with b.p. 127-130° (2 mm), $n^{20}D$ 1.5257.

The 2,4-dinitrophenylhydrazone of the ketone had m.p. 113-114°.

2,2,3,7-Tetramethyldodecatrien-3,7,9-one-11 (XIX). Over a period of 30 minutes, 5 g of diketene was added to a mixture of 9.7 g of 2,2,3,7-tetramethylnonen-3-yn-8-ol-7 and three drops of triethylamine at 70° and then the mixture was heated for a further two hours. The reaction product was pyrolyzed at 190-200° without preliminary treatment and distillation. Working up in the usual way and two vacuum distillations yielded 8.0 g (69%) of 2,2,3,7-tetramethyldodecatrien-3,7,9-one-11 with b.p. 128-134° (3 mm), $n^{20}D$ 1.5208.

The 2,4-dinitrophenylhydrazone had m.p. 115-117° and did not depress the melting point of the 2,4-dinitrophenylhydrazone of this ketone, obtained by method B.

SUMMARY

A series of new analogs of geranylacetone and pseudoionone were synthesized by three different methods.

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STEREOCHEMISTRY OF ACETYLENE SYNTHESIS WITH BICYCLIC KETONES

SYNTHESIS OF CIS-1-ETHYNYL-1-HYDROXY-6-DECALONE. ABSORPTION SPECTRA OF A SERIES OF TERTIARY α-DECALOLS

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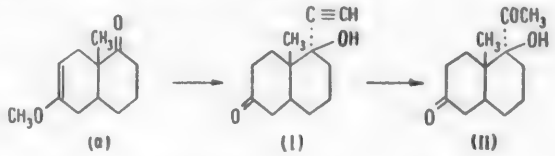
Over a number of years, a study has been made in our laboratory of the chemistry and stereochemistry of acetylene synthesis, including the condensation of acetylene with bicyclic ketones of the decalin series [1]. It was shown that, in a number of cases, this synthesis was stereospecific [2, 3]. Thus, starting from cis-9-methyl-methoxyoctalone (a), only one acetylene alcohol (I) was obtained.



(a) (I) (II)

The configuration of the substituents at C1 in alcohol (I) and its hydration product (II) was assigned on the basis of their reactivities [4].

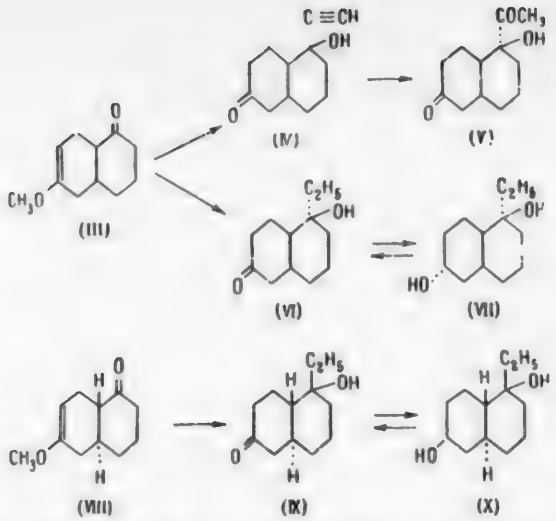
In the present work we accomplished the condensation of cis-methoxyoctalone (III) with sodium acetylide in liquid ammonia, which yielded, after hydrolysis, the acetylene alcohol (IV) as the main product and a small amount of the isomeric acetylene alcohols (IVa and IVb). It is possible that the latter were structural isomers, since the starting methoxyoctalone (III) could have contained the 7-methoxy isomer as an impurity [2]. Alcohol (IV) was characterized by the 2,4-dinitrophenylhydrazone and the absorption spectrum.

This condensation was previously accomplished by one of us by A.E. Favorskii's method, though the products were not investigated [5].

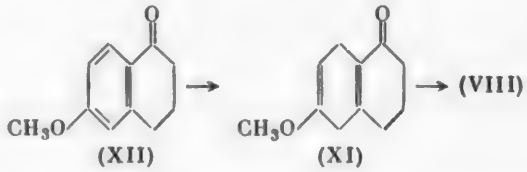
The acetylene alcohol (IV) was hydrated smoothly in methanol solution in the presence of mercuric sulfate to give the corresponding acetylhydroxydecalone (V), which formed a bis-2,4-dinitrophenylhydrazone. Judging by the ease of hydration of the acetylene alcohol (IV), and also by the fact that the acetylhydroxydecalone (V) obtained formed a bis-2,4-dinitrophenylhydrazone under the usual conditions, one can assume that both these compounds have the same steric disposition of the side chain and the hydroxyl at C1 as cis-ethynyldecalol (I) and its corresponding acetyl derivative (II).

Hydrogenation of the alcohol (IV) gave a good yield of a crystalline ethyldecalone (VI), which was reduced with lithium in liquid ammonia to give the diol (VII).

The action of ethylmagnesium bromide on the methoxy ketone (III) and subsequent hydrolysis yielded an oil, which was reduced with lithium in liquid ammonia to give a considerable amount of the ethyldiol (VII).

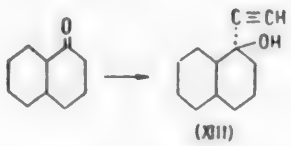


The action of ethylmagnesium iodide under the same conditions on the trans-methoxy ketone (VIII) yielded an oil, which was reduced with lithium in liquid ammonia to give the isomeric diol (X) as the main product. Oxidation of the latter with chromium trioxide yielded a crystalline ketol (IX), isomeric with the ketol (VI). The starting trans-methoxy ketone (VIII) was obtained as an oil by reduction of methoxyhexalone (XI) with lithium in liquid ammonia. The methoxyhexalone (XI) was synthesized by a known method from methoxytetralone (XII) [6].

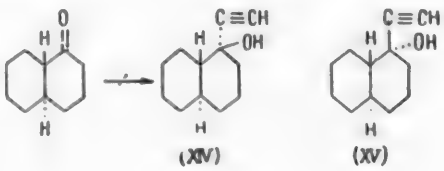


Since the keto alcohols (VI) and (IX) were obtained under identical conditions, one can assume that they differ from each other in the position of coupling of the rings, since in the case of preliminary isomerization of the cis-methoxyoctalone (III) into the trans-methoxyoctalone (VIII), the same product must be obtained in the two cases. Thus, the keto alcohol (VI) is a derivative of cis-decalin and, consequently, the acetylene alcohol (IV) and all its derivatives belong to this series, while the keto alcohol (IX) and the diol (X) are derivatives of trans-decalin.

As was shown recently, the condensation of acetylene with cis-α-decalone gives only one of the two possible acetylene alcohols; thus the synthesis proceeds also directly with the cis-form of the ketone as the acetylene alcohol (XIII) obtained is a derivative of cis-decalin [7].



In the condensation of acetylene with trans-α-decalone, two acetylene alcohols are formed and these are derivatives of trans-decalin.



The acetylene alcohols (XIII and XIV) were hydrated under mild conditions and their hydration products readily formed semicarbazones and a 2,4-dinitrophenylhydrazone (for XIV), while the ethynyldecalol (XV) required drastic conditions for hydration and a semicarbazone was obtained with difficulty from the acetyldecalol corresponding to it. Acetylation of the trans-ethynyldecalol (XIV) proceeded much more readily than the acetylation of the epimeric acetylene alcohol (XV). The cis-ethynyldecalol (XIII) was also acetylated under mild conditions. On the basis of acetylation data, it was assumed that in compounds (XIII) and (XIV) the hydroxyl group was in an equatorial position and in the acetylene alcohol (XV), it was in an axial position [7].

Thus, the three cis-α-ethynyldecalols (I, IV and XIII), obtained by one method, have similar chemical properties and apparently have identical steric structures at C1. The trans-α-ethynyldecalols (XIV) and (XV) differ from each other in the disposition of the substituents at C1, like their derivatives, the vinyl-ethyl- and acetyl-α-decalols.

In order to confirm this conclusion, we plotted the absorption spectra of the acetylene alcohols (I, IV and XIII-XV) and their reduction and hydration products in the region 900-1500 cm^{-1}.

The literature contains disconnected data on the absorption spectra of tertiary cyclic alcohols, referring to tertiary cyclohexanols and tertiary alcohols of the steroid series [8-12]. There is no information on the differences in the spectra of tertiary cyclic alcohols with different orientations of the hydroxyl groups. According to literature data, the bands pertaining to valence oscillations of the $\rightarrow$C$-$OH group of tertiary cyclic alcohols lie in the region 1100-1200 cm^{-1}. In the spectra we plotted of the compounds, a large number of bands of approximately equal intensity lay in the region 1000-1200 cm^{-1}. The absorption coefficient we calculated in this region for the most intense bands of certain alcohols, dissolved in carbon disulfide, equaled 40-50 units in most cases. From the low intensity of the absorption bands and their large number, it is difficult to say which of them pertain to $\rightarrow$C$-$OH valence oscillations. Despite this, we were able to show that compounds similar in chemical properties had similar spectra, while compounds with opposite configurations at C1 differed from each other.

Figure 1 shows absorption spectra of two epimeric series of trans-α-decalol derivatives. In comparing the general character of the spectra of the right and left series in the region 1000-1200 cm^{-1}, one notices a characteristic change in the transition from the spectra of the ethyl alcohols to the spectra of the acetylene alcohols.

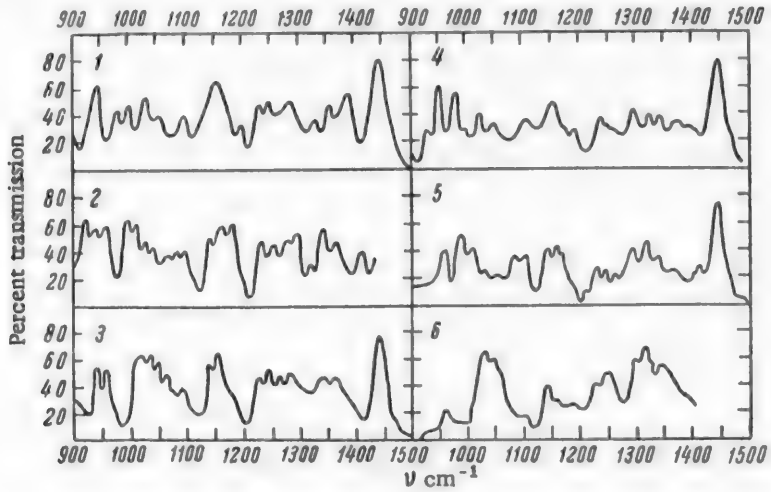
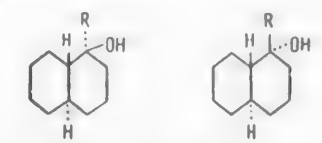


Fig. 1. Infrared absorption spectra of two epimeric series of trans-α-decalol derivatives.



1. — R = C_2H_5, 4. — R = C_2H_5,
2. — R = CH=CH_2, 5. — R = CH=CH_2.
3. (XIV) — R = C≡CH, 6. (XV) — R = C≡CH.

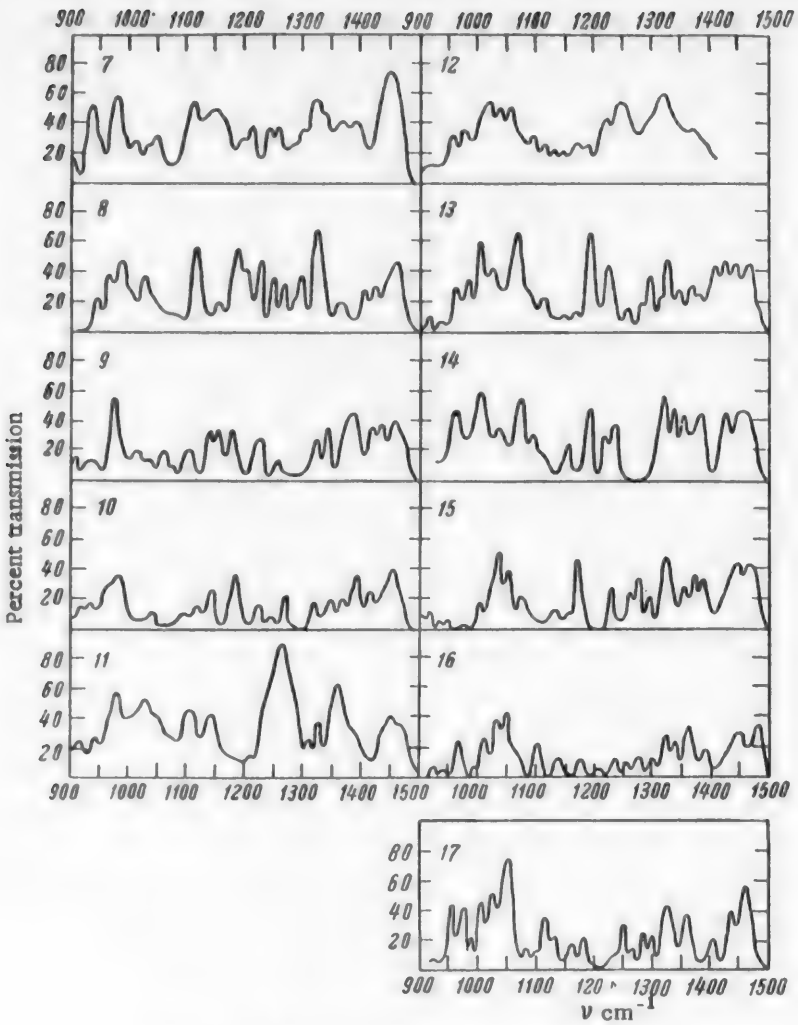
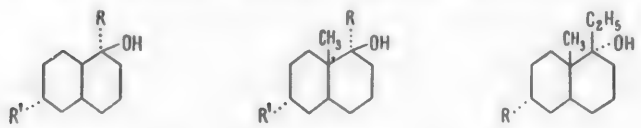


Fig. 2. Infrared spectra of cis-decalin derivatives.



7. — R = C_2H_5, R' = H,
8. (VI) — R = C_2H_5, R' = O,
12. (XIII) — R = C≡CH, R' = H,
13. (IV) — R = C≡CH, R' = O,
17. (VII) — R = C_2H_5, R' = OH.

9. — R = C_2H_5, R' = O,
14. (I) — R = C≡CH, R' = O,
16. — R = C_2H_5, R' = OH,
11. — R = C_2H_5, R' = OAc.

10. — R = O,
15. — R = OH.

While the most intense band at 1150 cm^{-1} and the band at 1100 cm^{-1} in the spectra of the ethyldecalols (1 and 4) are single, in the spectra of the vinyldecalols (2 and 5), these bands acquire a complex character and include 2-3 peaks. In the spectra of ethynyldecalols (3 and 6), these bands again become single. In going from the spectra of the ethyldecalols to the spectra of the ethynyldecalols, the intensity of the band at 1020-1050 cm^{-1} increases. It is interesting to note that the intensity of the absorption band at 1150 cm^{-1} increases. It is interesting to note that the intensity of the absorption band at 1150 cm^{-1} is considerably less in spectra (4-6) than in spectra (1-3). As was indicated above, on the basis of the chemical properties it was taken that in alcohol (XV) and in the vinyl- and ethyldecalols corresponding to it (spectra 4-6), the hydroxyl group has an axial disposition, while in alcohol (XIV) and its hydrogenation products (spectra 1-3), the hydroxyl group is oriented equatorially.

In the region 1200-1300 cm^{-1}, the similarity of the absorption spectra within the series (1-3) and (4-6) and the difference between spectra of the left and right series are observed.

The spectra of cis-decalin derivatives are illustrated in Fig. 2. As we indicated above, the acetylene alcohols (I, IV and XIII) were prepared in our laboratory by the same method from the corresponding cis-decalones. In comparing the absorption spectra (12-14), one observes the similarity between them and the difference from the spectra of the acetylene alcohols of the trans-series (3 and 6). In the region 1000-1100 cm^{-1}, the shapes of the spectra (13 and 14) are very similar, while in spectrum (12) the minima are less sharply expressed. In contrast to spectra (3-6), in the regions 1070-1200 and 1240-1300 cm^{-1} there are no intense bands in the spectra (12-14) and due to this, characteristic dips are formed. The spectra of the ethyldecalols of the cis-series (7-9, 11, 16 and 17), derived from the acetylene alcohols (I, IV and XIII) are characterized by the presence of an absorption band at about 1100 cm^{-1}. This band is absent from the spectra of ethyldecalols with the opposite configuration of the substituents at C_1 (10 and 15). In comparing the spectrum of the diol (17) with the spectra of epimeric diols with an angular methyl group (15 and 16), it was found that the spectrum (17) was very similar to spectrum (16) and differed from spectrum (15). In spectra (16 and 17), the most intense band in the region 1100-1200 cm^{-1} was the one at 1100 cm^{-1}. In spectrum (15), there was an extremely intense band at 1170 cm^{-1} in this range. Thus, the cis-ethynyldecalols (I, IV and XIII) and their derivatives, which are similar in chemical properties, have similar absorption spectra, indicating that these compounds have the same configuration at C_1. It is interesting to note that there is an intense absorption band at 980 cm^{-1} in the spectra of the ethyldecalols. Most of the cis-α-decalols with a 6-keto group and without it have an intense band at 1220 cm^{-1} in their spectra.

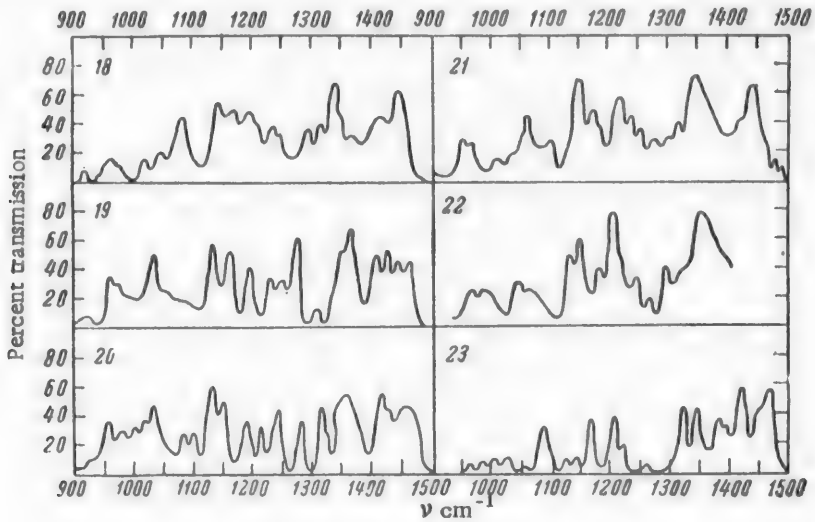
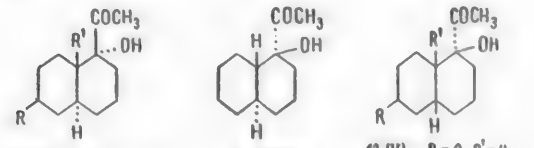


Fig. 3. Infrared spectra of cis- and trans-acetylhydroxyketodecalins.



18. (XVI) – R=H, R'=H,
20. (XVII) – R=O, R'=CH_3.

21. (XVIII)

19. (V) – R=O, R'=H,
22. (XIX) – R=H, R'=H,
23. (II) – R=O, R'=CH_3.

Figure 3 shows the spectra of acetyl derivatives of the cis and trans series, which we prepared by hydration of the corresponding acetylene alcohols (I, IV and XIII-XV) [4, 7]; they may be divided into two groups on the basis of the character of their spectra in the region 1100-1200 cm^{-1}. In this region, spectra (18-20) contain three bands. The most intense one of this series is the band at 1130 cm^{-1}. In spectra (21-23), the bands at 1150-1160 and 1207-1216 cm^{-1} are the most intense. Intense bands are absent from the region 1220-1320 cm^{-1} in the spectra (21-23) and a characteristic dip is formed.

Thus, the spectrum of the cis-acetyldecalol (22) is more similar to the spectrum of the trans-acetyldecalol (21) than to the spectrum of the epimeric trans-acetyldecalol (18), which agrees with the chemical behavior of these acetyldecalols. On the basis of their spectra, the acetyl compounds (V, XVI and XVII) may apparently be assigned to one configurational series and the acetyldecalols (II, XVIII and XIX) to the other. However, in its chemical properties, the acetyldecalol (V) is similar to compounds (II and XVIII). Since the spectrum of this substance was plotted with the material in the crystalline state, we cannot exclude the possibility that it exists in a converted form in the solid state.

EXPERIMENTAL

Cis-1-ethynyl-1-hydroxy-6-keto-Δ^5-octalin (IV). Into a three-necked flask, cooled with dry ice and acetone (−70°), was distilled 0.5 liter of dry, liquid ammonia. After the addition of 3 g of metallic sodium, about 30 liters of acetylene was passed into the flask over a period of one hour until the blue color disappeared. Then, with vigorous stirring, a solution of 10 g of cis-6-methoxy-1-keto-Δ^6-octalin (III) (b.p. 116-118° at 1.5 mm, $n^{20}D$ 1.5050) in 30 ml of absolute ether was added over a period of one hour. Stirring and the input of acetylene were continued for a further six hours and then 6 g of ammonium chloride was added and the solution left overnight. On the following day, water was added and the solution extracted with ether. After evaporation of the ether, the residual oil was shaken for two hours with 10 ml of 10% hydrochloric acid. We obtained 3 g of ketone (IV) with m.p. 154-155° (from 50% aqueous methanol).

Found %: C 75.00, 75.07; H 8.26, 8.40. $C_{12}H_{16}O_2$. Calculated %: C 75.00; H 8.33.

The 2,4-dinitrophenylhydrazone of (IV) had m.p. 161-162° (from alcohol).

Found %: N 15.02, 15.06. $C_{18}H_{20}O_5N_4$. Calculated %: N 15.04.

By fractional crystallization, from the mother solution we obtained the isomeric ketol (IVa) with m.p. 177-178° (from aqueous methanol).

Found %: C 74.63, 74.46; H 8.40, 8.46. $C_{12}H_{16}O_2$. Calculated %: C 75.00; H 8.33.

By recrystallization and freezing the oil left after separation of the two isomers described above, we obtained 50 mg of isomer (IVb) with m.p. 133-135° (from aqueous methanol).

Found %: C 75.11, 75.16; H 8.26, 8.38. $C_{12}H_{16}O_2$. Calculated %: C 75.00; H 8.33.

Hydration of acetylene alcohol (IV). 2 g of the acetylene alcohol was dissolved in 48 ml of methanol and 4 ml of water added; then, while the solution was heated and stirred, 0.6 g of finely ground mercuric sulfate was added to it in portions. The reaction was continued for six hours at 58-60°, when metallic mercury partially separated and then the reaction was continued for a further five hours while the solution was boiled. After the usual treatment [4] and chromatography, from the benzene fraction we obtained 1.3 g of cis-1-acetyl-1-hydroxy-6-ketodecalin (V) with m.p. 74-75° (from benzene with petroleum ether).

Found %: C 68.61, 68.59; H 8.68, 8.73. $C_{12}H_{18}O_3$. Calculated %: C 68.54; H 8.63.

The bis-2,4-dinitrophenylhydrazone of (V) was yellow and melted at 157-158° (from alcohol).

Found %: N 19.70, 19.86. $C_{24}H_{26}O_9N_8$. Calculated %: N 19.65.

Cis-1-ethyl-1-hydroxy-6-ketodecalin (VI). 0.96 g of acetylene alcohol (IV) was hydrogenated exhaustively in alcohol solution in the presence of palladium on calcium carbonate. About 250 ml of hydrogen was absorbed. After removing the solvent and recrystallizing the residue from a mixture of ether and petroleum ether, we obtained 0.8 g of ketol (VI) with m.p. 77-78°.

Found %: C 73.63, 73.68; H 10.30, 10.17. $C_{12}H_{20}O_2$. Calculated %: C 73.42; H 10.28.

The golden 2,4-dinitrophenylhydrazone of (VI) melted at 150.5-151.5° (from alcohol).

Found %: N 14.64, 14.68. $C_{18}H_{24}O_5N_4$. Calculated %: N 14.89.

Cis-1-ethyl-1,6-dihydroxydecalin (VII). a) A solution of 2.2 g of the keto alcohol (VI) in 15 ml of dry ether was poured into a solution of 1 g of lithium in 120 ml of liquid ammonia and then about 20 ml of ethyl alcohol was added dropwise (until the solution was decolorized). We obtained 1.5 g of diol (VII) with m.p. 161.5-162° (from alcohol).

Found %: C 72.72, 72.68; H 11.13. $C_{12}H_{22}O_2$. Calculated %: C 72.68; H 11.13.

b) An ether solution of 3.4 g of cis-methoxyoctalone (III) was added to an ether solution of ethylmagnesium bromide, prepared from 0.9 g of magnesium and 4 g of ethyl bromide. After working the product up and chromatographing it, from the benzene fraction we obtained 2.6 g of an oil, which was reduced with 1.1 g of lithium in 120 ml of liquid ammonia in the presence of alcohol. We obtained 2.7 g of a crystallizable oil, which yielded 1.4 g of ethyldiol (VII) with m.p. 160-161°. A mixed melting point with the diol from experiment "a" was not depressed.

Trans-1-ethyl-1,6-dihydroxydecalin (X). 1.5 g of trans-6-methoxy-Δ^6-octalone (VIII), prepared by reducing 2 g of methoxyhexalone (XI) with 0.5 g of lithium in liquid ammonia, was added to an ether solution of ethylmagnesium iodide, prepared from 0.4 g of magnesium and 2.6 g of ethyl iodide. Working up yielded 1.4 g of oil. After chromatography, the benzene fraction gave 1 g of an oil, which was reduced with lithium in liquid ammonia, as described above. We obtained diol (X) with m.p. 113-114°; ν 1018, 1057, 1101 cm^{-1}.

Found %: C 72.69, 72.48; H 11.16, 11.17. $C_{12}H_{22}O_2$. Calculated %: C 72.68; H 11.18.

Trans-1-ethyl-1-hydroxy-6-ketodecalin (IX). 150 g of diol (X) was oxidized with chromium trioxide in acetic acid. We obtained 80 mg of ketol (IX) with m.p. 72-73° (from ether and petroleum ether); ν 1132, 1150 cm^{-1}.

Found %: C 73.65, 73.85; H 10.26, 10.27. $C_{12}H_{20}O_2$. Calculated %: C 73.42; H 10.28.

A mixture with ketol (VI) melted at 52-54°.

The absorption spectra were plotted on an IKS-2 double-beam infrared spectrophotometer with an NaCl prism. The resolving power of the apparatus in the range 800-1200 cm^{-1} was 5-8 cm and at 1200-1500 cm^{-1}, it was 8-15 cm.

The spectra of substances (XIII, XV and XIX) were plotted with the materials in carbon disulfide solution in a cell 1 mm thick with a concentration of $7 \cdot 10^{-2}$. The other substances whose spectra are presented in Fig. 1, cis-ethyldecalol (spectrum 7) and the acetyldecalols (XVI) and (XVIII) were examined in the liquid state in a cell 0.01 mm thick. The rest of the spectra were plotted with the substances in the crystalline state as a paste in vaseline oil. The film thickness was about 0.01 mm.

SUMMARY

1. It was shown that the condensation of cis-6-methoxy-Δ^6-octalone with sodium acetylide in liquid ammonia forms cis-1-ethynyl-1-hydroxy-6-keto-Δ^5-octalin, a derivative of cis-decalin.

2. A series of substituted cis- and trans-α-decalols were prepared.

3. The absorption spectra of a series of tertiary α-decalols are given and it was shown that the cis-ethynyl-α-decalols, obtained by the one method, are similar in their chemical properties and have similar absorption spectra in the region 1000-1350 cm^{-1}.

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INFRARED ABSORPTION SPECTRA OF SUBSTITUTED TRANS-1,6-DECALINDIOLS AND Δ^5-1,6-OCTALINDIOLS

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As we reported previously, in studying the reduction of a series of substituted hydroxy-β-decalinones with lithium in liquid ammonia and sodium boron hydride, we obtained a series of decalindiols containing a secondary hydroxyl group at C_6 and a tertiary hydroxyl group at C_1 [1-3]. The diols obtained in this way were simultaneously derivatives of secondary β-decalols and tertiary α-decalols.

In the literature there are quite detailed descriptions of the absorption spectra of secondary β-decalols and their derivatives, which include 3-hydroxysteroids. Differences were also found in the spectra of β-decalols with different steric orientations of the hydroxyl groups. It was found that the absorption spectra of secondary cyclic alcohols had intense bands in the region 1000-1050 cm^{-1}, corresponding to C—OH valence oscillations; thus, the absorption spectra of trans-β-decalols with an equatorial disposition of the hydroxyl group and of 3-β-hydroxysteroids with trans-linking of rings A/B were characterized by the presence of bands close to 1050 cm^{-1}, while the absorption spectra of β-decalols with an axial disposition of the hydroxyl group and of 3-α-hydroxysteroids with trans-linking of the rings A/B were characterized by the presence of bands close to 1000 cm^{-1}. The absorption spectra of acetates of β-decalols and 3-hydroxysteroids with an equatorial hydroxyl group contained an extremely intense single absorption band in the region of 1250 cm^{-1}, while the spectra of acetates of 3-hydroxysteroids and β-decalols with an axial hydroxyl group (regardless of the configuration of compound at the union of rings A and B) have a complex peak consisting of several bands [4, 5]. The literature contains only fragmentary data on the absorption spectra of tertiary α-decalols [3].

In the present report we present the absorption spectra of 1-substituted-trans-9-methyl-1,6-decalindiols (I, II and III) (1-3), 9-methyl-Δ^5-1,6-octalindiols (X, XI and XII) (10-12) and their 6-monoacetates (IV, V, VI, XIII, XIV and XV) (4-6 and 13-15) and also the absorption spectra of the starting keto alcohols (VII-IX and XVI-XVIII) (7-9 and 16-18), not containing a secondary hydroxyl group, plotted in the region 900-1500 cm^{-1}. All these compounds (I-XVIII),* as tertiary α-decalols, have the same configuration of the substituents at C_1, since they were all prepared from the acetylene alcohol (XVIII). Diols (I-III and X-XII) contain the same steric orientation of the secondary hydroxyl group, since hydrogenation of the unsaturated alcohols (II, III and X-XII) gave the same diol (I) in each case.

Figure 1 shows the absorption spectra of trans-9-methyldecalin derivatives. A comparison of the spectra presented shows the sharp difference between the spectra of ketones, alcohols and acetates. The spectra of the ketones (7-9) contain a collection of bands of approximately equal intensity. In the range 1200-1300 cm^{-1} they have a characteristic pattern of two intense peaks. In the range 1100-1200 cm^{-1} there is a collection of quite intense bands at 1110-1125, 1140-1150 and 1175-1185 cm^{-1}. The band at 1150 cm^{-1} is absent from the last spectrum. In the region 1000-1100 cm^{-1}, an increase in the intensity of the bands is observed in going from the spectrum of ethyldecalol (VII) to that of ethynyldecalol. Intense bands are absent from the spectra of the diols (1, 2 and 3) in the range 1100-1300 cm^{-1} and, due to this, a characteristic dip is formed. The spectra of the diols

* The spectra are numbered with Arabic numerals and the compounds with the corresponding Roman numerals.

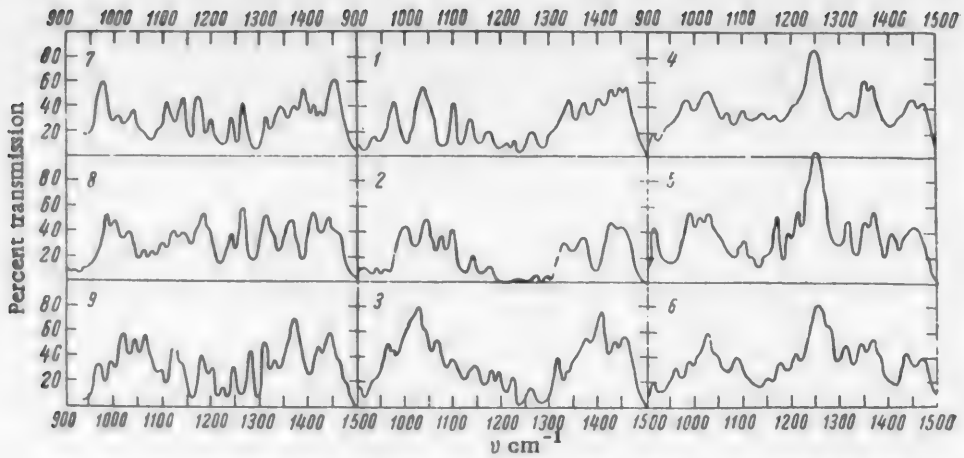
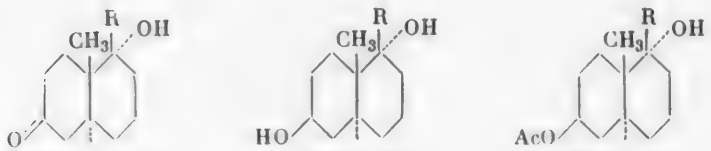
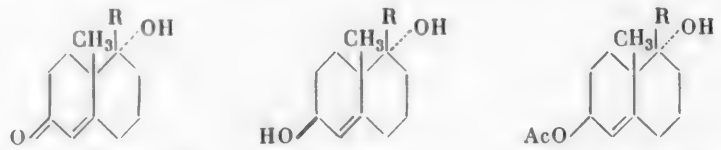


Fig. 1. Infrared spectra of trans-9-methyldecalin derivatives. Explanation in text.



have three bands in the range 1100-1200 cm^{-1}. In going from the spectrum of ethyldiol (1) to that of vinyldiol (2) and then that of ethynyldiol (3), not only the frequencies (1100, 1140 and 1175 cm^{-1}),but also the character of the intensity ratios are preserved. In the region 1000-1100 cm^{-1}, the spectra of all the diols show an intense peak, corresponding to C—OH oscillations of the secondary hydroxyl group. In the region 1050-1200 cm^{-1}, the spectra of the acetates (4 and 6) are characterized by the absence of intense bands and only in spectrum (5) is there one intense peak at 1170 cm^{-1} in this region. In the region 1000-1050 cm^{-1}, like the spectra of the diols, the spectra of the acetates have intense bands corresponding to the C—OCO oscillations. The spectra of the acetates differ sharply from the spectra of the keto alcohols (7-9) and the diols (1-3) in the presence of an extremely intense band at about 1250 cm^{-1}, characteristic of acetates.

Figure 2 shows the absorption spectra of 9-methyl-Δ^5-octalin derivatives. These spectra maintain the same general pattern of the spectra illustrated in Fig. 1. In the region 1200-1300 cm^{-1}, the spectra of the keto alcohols (16-18) have three absorption bands.



In the region 1100-1200 cm^{-1}, the spectra (16-17), like the spectra (7 and 8), have three quite intense bands. Like spectra (7-9), spectra (16-18) show an increase in the intensity of the bands in the range 1000-1100 cm^{-1} in going from the spectrum of ethyloctalol (16) to the spectrum of ethynyloctalol (18). Like the spectra of diols (1-3), the spectra of diols (10-12) retain a characteristic dip in the region 1100-1300 cm^{-1}; however, in contrast to spectra (1-3), spectra (10-12) have a peak at about 1200 cm^{-1}. The shapes of the spectra of the acetylene alcohols (3 and 12), which have two extremely intense peaks at about 1030 and 1400 cm^{-1}, are very strikingly similar. The spectra of the acetates of the unsaturated alcohols (13-15) are also very similar to the corresponding spectra of the acetates of the trans-series (4-6). Thus, the two series of compounds (I-IX) and

(X-XVIII) with the same disposition of the substituents and similar spectra apparently have the same conformation and, consequently, the angular methyl group in compounds (X-XVIII) has an axial disposition. In the range 1200-1450 cm^{-1}, the spectra presented have a collection of intense bands, observed in the spectra of compounds with CH_2 and CH_3 groups. The presence of these bands is connected with different types of deformation oscillations of the methylene group. The most intense band, belonging to the deformation oscillation of the CH_2 group and the asymmetric deformation oscillation of the CH_3 group, is observed at about 1460 cm^{-1}. There are also intense absorption bands at about 1435, 1410 and 1370 cm^{-1} and below.

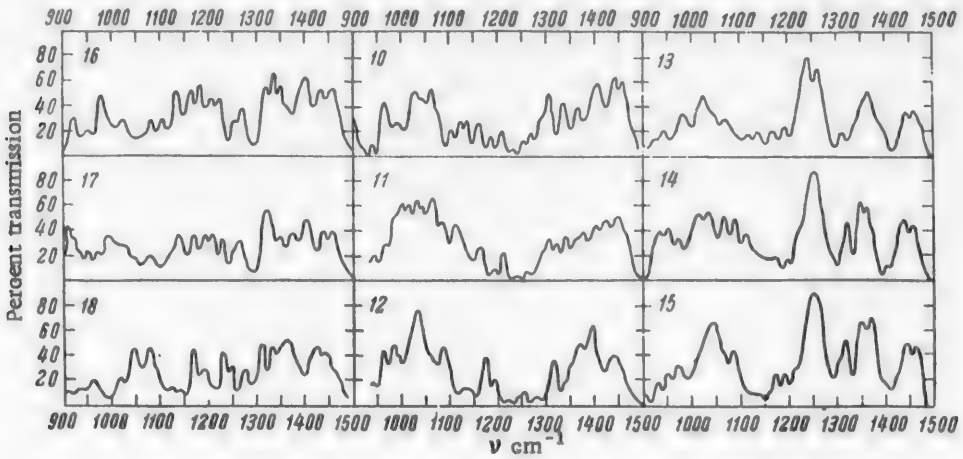
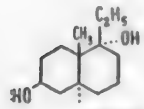
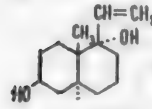
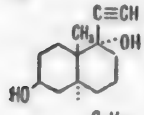
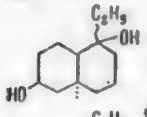
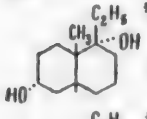
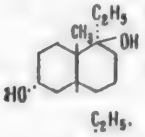
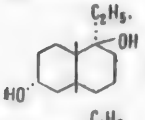
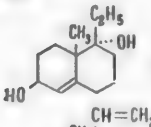
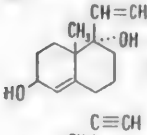
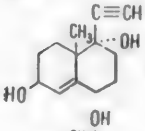
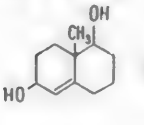


Fig. 2. Infrared spectra of 9-methyl-Δ^5-octalin derivatives. Explanation in text.

As was previously noted [3], there is a band at 980 cm^{-1} in the spectra of ethyl alcohols. In the spectra of the vinyl alcohols, there is an absorption band at 990 cm^{-1}, characteristic of compounds of the type $RCH{=}CH_2$. For examining the steric disposition of the secondary hydroxyl groups in the diols, in the table are given the characteristic frequencies of the C−OH valence oscillations of the secondary hydroxyl groups of the diols (I-III and X-XII) and the frequencies of the C−OCO and C−C−OC oscillations of the corresponding acetates and also the

spectra of the series of diols (XIX-XXIII), which we described previously [3, 6].

The data in the table show that the spectra of trans-decalindiols (I-III) have one intense absorption band in the region 1050-1030 cm^{-1}, which agrees with literature data for the spectra of trans-β-decalols with an equatorial hydroxyl group. In the spectrum of the diol of the cis-series (XX), the most intense absorption band is at about 1030 cm^{-1}. The spectra of the cis-decalindiols (XXI and XXII) are characterized in this region by three intense absorption bands at about 1050, 1030 and 1005 cm^{-1}. In both cases, the band at 1050 cm^{-1} is the most intense. The spectra of the unsaturated diols (X and XI) have several absorption bands of equal intensity in the region 1065-1000 cm^{-1}. The spectra of the acetylene alcohols (III and XII) have a single peak, which is slightly displaced into the region of lower frequencies. In this region, the spectra of the alcohols (XIX-XXIII) have two bands; however, in both cases, the most intense peaks are those at about 1050 cm^{-1}. The extremely high intensity of the band at 1057 cm^{-1} in the spectrum of the diol (XXIII) is apparently connected with the presence of two equatorial hydroxyl groups in this diol. In the spectra of the acetates, the band corresponding to C−OCO oscillations and corresponding to the C−OH oscillations in the spectra of the original alcohols (I-III and X) is displaced somewhat toward lower frequencies relative to the absorption bands of the latter. According to literature data for the spectra of 3-hydroxysteroids and their corresponding acetates with an equatorial hydroxyl group and trans-coupling of the rings A/B, this displacement occurs in the same direction. On the contrary, in the corresponding compounds with an axial hydroxyl group, the frequency of the C−OCO oscillation of the acetates is higher than the C−OH frequency of the alcohols [5]. Only in the acetate of diol (XII) is the frequency of the C−OCO oscillation higher than the frequency of the C−OH oscillation in the diol itself. The extremely intense single absorption band of CO−C−C in the spectra of the acetates of alcohols (I, II, XI, XII and XXI) lies in the

Formula and compound No.	Frequency (cm^{-1})		
	C—OH	C—OCO	$-\overset{\overset{O}{\|\|}}{C}-OC$
 (I)	1043	1026	1247
 (II)	1048	1031 1010	1241
 (III)	1029	1025	1276 1257
 (XIX)	1057 1018		
 (XX)	1050 1032		
 (XXI)	1044 1031 1010	1029	1261
 (XXII)	1050 1027 1005		
 (X)	1064 1047 1035	1025	1262 1239
 (XI)	1067—1036 1016 1005	1066 1031—1026	1250
 (XII)	1036	1045	1252
 (XXIII)	1054 1026		

*Alcohols (XX) and (XXI) are stereoisomers with respect to the position of the substituents at C_1.

region 1260-1240 cm^{-1}, which is characteristic of the spectra of β-decalols with equatorial hydroxyl groups. In this region, besides the basic peak, the spectra of the acetates of alcohols (III and X) have a less intense additional peak. Thus, the spectra of the diols (I-III, X-XII, XIX, XXI-XXIII) and the acetates corresponding to them indicate an equatorial disposition for the secondary hydroxyl groups in these compounds, which confirms the conclusions at which we arrived previously on the structure of 1,6-decalindiols [2].

EXPERIMENTAL

The spectra of the tertiary α-decalols (1-18), like the spectra we obtained previously [3], were plotted on a double-beam infrared spectrophotometer, IKS-2, with an NaCl prism in the region 900-1500 cm^{-1}. Onto the recording apparatus was mounted a calibration marker, connected to the wavelength drum. The spectra were plotted at a rate of 11.5 cm^{-1}/min on a scale of 1.76 cm^{-1}/mm. The accuracy with which the frequency scale was marked out on the spectrum by the calibration marker was not less than ±2 cm^{-1} under these conditions.

The apparatus was calibrated in the region 800-1900 cm^{-1} by means of the ammonia and atmospheric water spectra. The resolving power of the apparatus in the range 800-1200 cm^{-1} was 5-8 cm^{-1} and from 1200-1500 cm^{-1}, 8-15 cm^{-1}. The slits were opened automatically during plotting of the spectra and the slit widths were reduced by a factor of two in comparison with the slit widths of the apparatus issued by the factory.

To calibrate the IKS-2 from the atmospheric water spectrum, we made use of the possibility of converting the apparatus to single-beam recording. For this purpose, the constant aperture channel was shut off and the following system balanced by applying the required bias potentials to the cathode of the 6P6 tube of the cathode follower in unit No. 3 with the potentiometer of the "balance of the synchronous detector" on the control panel. In converting the apparatus to the double-beam system, the following system had to be balanced again. It was more convenient to apply the bias potential directly from the anode of the corresponding 6P6 tube onto its grid through a divider with a resistance of not less than 1.5 MΩ. The voltage divider was disconnected from the anode of the tube and its grid by means of one triple tumbler. Under these conditions, the following system of the IKS-2 maintained a constant amount of radiation energy falling on the bolometer. The spectrum was obtained with the intensities of the absorption bands reversed with respect to double-beam recording.

Since most of the substances were sparingly soluble in carbon disulfide, the spectra of all the substances were plotted with the materials in a crystalline state as a paste in vaseline oil. The film thickness was approximately 0.01 mm. Into the balancing beam was placed a cell with a layer of vaseline oil of the chosen thickness.

SUMMARY

1. The absorption spectra of a series of substituted 1,6-decalindiols, Δ^5-1,6-octalindiols and their acetates and the 6-keto alcohols corresponding to them in the region 900-1500 cm^{-1} are presented and described.

2. By means of the absorption spectra of 1-ethyl-, 1-vinyl- and 1-ethynyl-substituted 9-methyl-1,6-decalindiols, 9-methyl-Δ^5-octalindiol and its 1-ethyl, 1-vinyl and 1-ethynyl derivatives and the spectra of their acetates, it was shown that these compounds contained an equatorial secondary hydroxy group.

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*Original Russian pagination. See C.B. translation.

**See C.B. translation.

SYNTHESIS OF DIENES WITH A FIXED TRANSOID DISPOSITION OF THE DOUBLE BONDS

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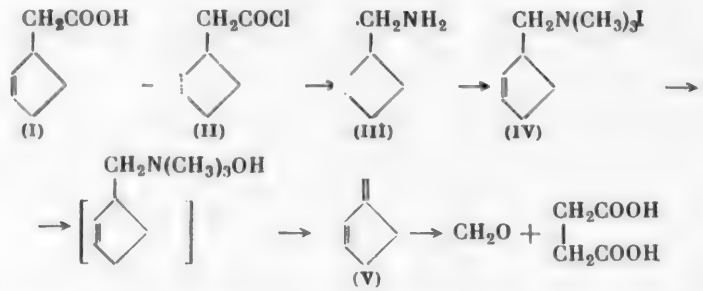
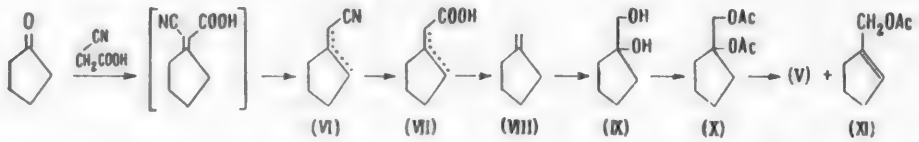
Institute of Organic Chemistry, Academy of Sciences, USSR

In continuing work begun previously [1] on the synthesis of cyclic dienes with a fixed transoid disposition of the double bonds, we developed a method of synthesizing methylenecyclopentene (V) by the following scheme:



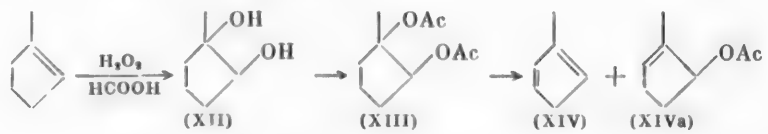
Methylenecyclopentene (V) is a compound with very much lower stability than methylenecyclohexene (XVIII), is readily oxidized in air, and gradually polymerizes on standing in a sealed ampoule, even in the presence of stabilizers. It does not give crystalline adducts with maleic anhydride and benzoquinone. When ozonized it forms formaldehyde and succinic acid.

We also developed another method of synthesizing methylenecyclopentene by the scheme

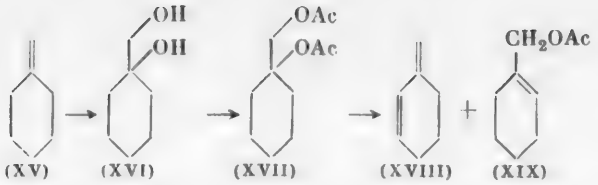


The samples of methylenecyclopentene (V) obtained by the different methods were found to be identical (by the spectra and other physical constants and also from the ozonization products).

The pyrolysis of the diacetate (XIII), obtained from methylcyclopentene, yielded 2-methylcyclopentadiene (XIV), whose structure was proved by its adduct with maleic anhydride and the ultraviolet spectrum, and also the monoacetate (XIVa), whose structure was not proved.

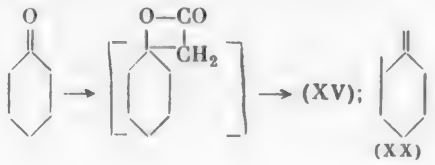


We also studied possible methods of synthesizing methylenecyclohexene (XVIII). In order to synthesize methylenecyclohexene by a scheme analogous to the preparation of methylenecyclopentene by the pyrolysis of the diacetates, it was necessary to develop a convenient method of synthesizing methylenecyclohexane (XV).



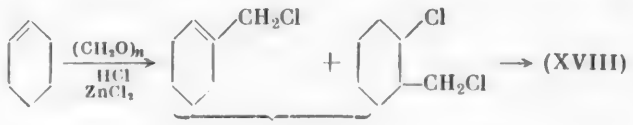
After a detailed study of the reactions of cyclohexanone with ketene in the presence of various catalysts, we were able to find suitable conditions for the synthesis of (XV) in good yield.

The cyclohexanone was condensed with ketene in an ether medium in the presence of boron trifluoride etherate to yield a β-lactone, which was decarboxylated by heating to 110° to give (XV) in about 60% yield.



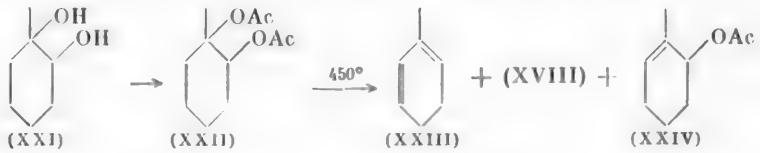
In passing, we also studied the condensation of ketene with 2-methylcyclohexanone, cyclohexenone and cyclopentanone and pyrolysis of the lactones formed gave 2-methylmethylenecyclohexane (XX), methylenecyclohexene (XVIII) and methylenecyclopentane (VIII) in yields of only 40, 10 and 15%, respectively. The glycol (XVI), obtained by oxidation of methylenecyclohexane (XV), was converted into the diacetate (XVII). At 500°, the diacetate obtained gave a mixture of methylenecyclohexene (XVIII) and the acetate of cyclohexenylmethanol (XIX). The methylenecyclohexene (XVIII) obtained by this method was found to be identical in its physical constants with samples of (XVIII), which we prepared previously by other methods [1].

Chloromethylation of cyclohexene in the presence of zinc chloride at 55-60° gave a mixture of chlorides.



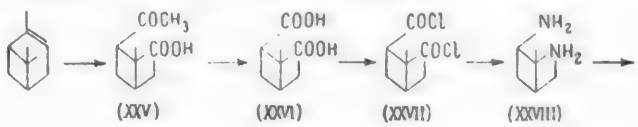
Elimination of hydrogen chloride from the mixture of chlorides with potassium hydroxide in boiling ethylene glycol also produced methylenecyclohexene (XVIII) in a total yield of about 40%.

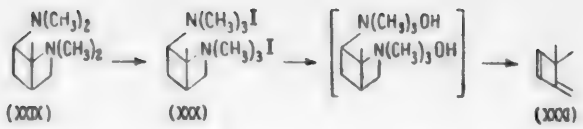
We also studied the pyrolysis of the diacetate (XXII), obtained by the following scheme:



It was found that in contrast to the pyrolysis of its cyclopentane analog (XIII), the pyrolysis of (XXII) gave a mixture of methylenecyclohexene (XVIII) and 2-methylcyclohexadiene (XXIII) in a ratio of 1:1. By treatment of the mixture obtained with maleic anhydride, it was possible to isolate methylenecyclohexene (XVIII), with which maleic anhydride did not react, and also the adduct of 2-methylcyclohexadiene with maleic anhydride.

We also developed a method of synthesizing a diene with a transoid system of double bonds connected to a cyclobutane ring, 2,3-dimethylmethylenecyclobutene (XXXI) by the following scheme (a synthesis of (XXXI) by similar methods was recently published in the literature [3]):

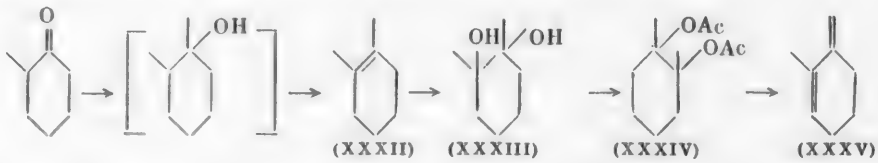




The spectra and other constants of (XXXI) were identical with those described in the literature [3].

None of the dienes we described with a fixed transoid disposition of the double bonds, apart from (XXXV) described below, gave crystalline adducts with maleic anhydride or benzoquinone (at 25 and 100°).

In studying the pyrolysis reactions of the acetates of various cyclic glycols and alcohols, we also studied the pyrolysis of the diacetate (XXXIV). We prepared the latter by the general scheme, starting from Δ^1-1,2-dimethylcyclohexene (XXXII), which was prepared from 2-methylcyclohexanone.



It was found that pyrolysis of (XXXII) formed 2-methylmethylenecyclohexene (XXXV) and also a monoacetate, whose structure was not established. The position of the absorption maximum in the ultraviolet indicated a transoid disposition of the double bonds. The structure of (XXXV) was proved by its oxidation with permanganate in the cold, which yielded glutaric acid (65%). The hydrocarbon obtained gave a crystalline adduct with maleic anhydride (about 50%), whose structure has not as yet been established.

EXPERIMENTAL

All the pyrolysis reactions were performed in a pyrex tube (18-mm diameter and the heated section 40 cm long) filled with pyrex rings (2-mm diameter).

Preparation of (Δ^2-cyclopentenylmethyl)-amine (III). With vigorous stirring and cooling to 0°, a solution of 116 g of the acid chloride (II), obtained from (I) by the action of phosphorus trichloride [2], in 350 ml of ether was added over a period of two hours to a solution of 88 g of sodium azide in 200 ml of water. The solution was stirred for a further two hours and then the ether layer separated, washed with 5% sodium bicarbonate solution and water and added dropwise to boiling benzene (350 ml) over a period of three hours. After the addition, the benzene solution was boiled for a further one hour until the evolution of nitrogen ceased and was then added dropwise to 500 ml of boiling HCl over a period of four hours. Boiling was continued for a further one hour until the evolution of carbon dioxide ceased. The aqueous layer was evaporated to dryness in vacuum and the residue decomposed with excess 30% sodium hydroxide. The layer of amine liberated was dried with solid sodium hydroxide and distilled. We thus obtained 49 g of amine (III) with b.p. 134° (747 mm), $n^{21}D$ 1.4750.

Found %: N 14.75, 14.83. $C_6H_{11}N$. Calculated %: N 14.30.

The picrate had m.p. 118-119°.

Methylation of amine (III). 71 g of methyl iodide was added at 0° to a solution of 49 g of the amine in 100 ml of methanol and then with stirring, a further 71 g of methyl iodide was added, followed by a solution of 20 g of sodium hydroxide in 100 ml of methanol, with cooling; after two hours, 71 g of methyl iodide was again added and then another solution of 20 g of sodium hydroxide in 100 ml of methanol. The operation was performed two more times and then, on the following day, the solution was boiled under reflux until it was neutral to litmus. The methanol was evaporated and the residue dissolved in a small amount of water. The solution was poured into 150 ml of 35% sodium hydroxide solution and the methiodide (IV) liberated was separated and recrystallized from a mixture of acetone and methanol. We obtained 133 g (100%) of the methiodide (IV) with m.p. 188-189° (decomp.).

Found %: N 5.51, 5.49. $C_9H_{18}NI$. Calculated %: N 5.24.

Preparation of methylenecyclopentene (V). With stirring and cooling in ice, a solution of 100 g of methiodide (IV), in 300 ml of water and 50 ml of methanol, was added to freshly precipitated silver oxide (prepared from 144 g of silver nitrate and 50 g of potassium hydroxide) and 100 ml of water. The reaction mixture was stirred at room temperature for two hours and then left overnight. The solution of reaction products was separated from the silver salts, which were washed with 50 ml of water. The filtrate and wash water were evaporated in vacuum at a temperature not exceeding 55° and the residue was pyrolyzed by heating to 140-150° in a vacuum of 45 mm. The reaction products were collected in a trap (cooled with a mixture of acetone and dry ice). The mixture of reaction products was poured onto ice and the hydrocarbon layer separated, dried with potassium carbonate and distilled on a column; this yielded 25 g (57.6%) of methylenecyclopentene (V).

B.p. 79-79.5° (750 mm), $n^{20}D$ 1.4850, λ_{max} 234 mμ, ε 14300 (heptane); IR-spectrum (in CCl_4): 1000, 1100, 1140, 1280, 1450, 1630 cm^{-1}.

Found %: C 89.80, 89.70; H 10.00, 10.20. C_6H_8. Calculated %: C 90.00; H 10.10.

The hydrocarbon was extremely readily oxidized in air and gave a polymer with maleic anhydride at 25 and 100° and quinhydrone with benzoquinone. Attempts to condense it with acrylonitrile at 150° [as in the case of methylenecyclopentane (VIII)] proceeded with explosive decomposition.

Ozonization of methylenecyclopentene (V). 1 g of methylenecyclopentene in 35 ml of ethyl acetate was ozonized with a stream of ozonized oxygen (0.01 m/hour) for five hours at −40°. 17 ml of the ozonide solution obtained was hydrogenated in a long-necked flask with PtO_2 until the absorption of hydrogen ceased. The formaldehyde content was determined by distillation into a solution of 1.2 g of dinitrophenylhydrazine in 50 ml of methanol and 1 ml of concentrated sulfuric acid. The crystals (0.92 g) isolated melted at 160-161° (from methanol) and did not depress the melting point of an authentic sample. To the residual solution of ozonide was added 3 ml of 90% peracetic acid and then the solution was heated at 60° for four hours. The ethyl acetate and acetic acid were distilled off in vacuum and the succinic acid isolated (0.5 g) had m.p. 180-181° (from water) and did not depress the melting point of an authentic sample.

Synthesis of a mixture of cyclopenteneacetic acids (VII). a) 316 g of cyclopentanone, 290 g of cyanoacetic acid, 40 ml of piperidine and 240 ml of benzene were heated together to 160°. The water liberated during the reaction was separated with a water separator. The mixture was boiled until the separation of water ceased. After cooling, the reaction mixture was washed with water, dilute hydrochloric acid, and then 5% sodium bicarbonate solution. The residue after evaporation of the benzene was vacuum distilled. We thus obtained 300 g (76%) of a mixture of nitriles (VI) with b.p. 90-92° (25 mm).

b) The mixture of nitriles (VI) was hydrolyzed by boiling with sodium hydroxide solution (230 g in 1 liter of water) for ten hours until the evolution of ammonia ceased. The reaction product was acidified with 800 ml of concentrated hydrochloric acid with cooling and the liberated oily layer extracted with ether, washed carefully with 5% sodium acetate solution and water, and dried with calcium chloride. After removal of the ether, the residue (300 g) crystallized and had m.p. 50-53°.

Preparation of methylenecyclopentane (VIII). In the decarboxylation of the mixture of acids (VII), methylenecyclopentane (VIII) was obtained in exactly the same yield from the crude material as from the redistilled mixture of acids (VII) and, therefore, the crude mixture of acids (VII) was used for the pyrolysis. 200 g of this mixture of acids (VII) was heated in a Wurtz flask so that the temperature of the emergent vapors did not exceed 105°. The distillate obtained was washed with 10% sodium carbonate solution, dried, and distilled on a column. We obtained 100 g (78%) of methylenecyclopentane (VIII) with b.p. 72.5-73° (750 mm), $n^{17}D$ 1.4362.

Oxidation of methylenecyclopentane (VIII). 100 g of (VIII) was added dropwise to a stirred solution of 250 g of 30% hydrogen peroxide and 800 ml of 85% formic acid at 30-35°. The reaction mixture was left overnight and then the residue (after removal of the water and formic acid in vacuum) was stirred at 45° with 600 ml of 20% sodium hydroxide. The solution of reaction products was saturated with potassium carbonate, the layer of liberated glycol separated and the aqueous layer further extracted with ethanol. The combined extracts were dried with potassium carbonate and the residue after removal of the ethanol was vacuum distilled. We obtained 110 g of glycol (IX) with b.p. 122-128° (20 mm), which crystallized in the receiver; the m.p. was 38° (from petroleum ether with b.p. 60-80°). The literature reports m.p. 39-41° [4].

Acetylation of glycol (IX). 250 g of acetyl chloride was added dropwise to a stirred mixture of 110 g of glycol, 200 ml of ether and 450 g of dimethylaniline. After the addition, the reaction mixture was boiled under reflux for three hours and then poured into water. The layer which separated was washed with 10% hydrochloric acid to an acid reaction to Congo and with 5% sodium bicarbonate solution and dried with magnesium sulfate. Vacuum distillation yielded 165 g of diacetate (X) with b.p. 119-123° (17 mm), $n^{21}D$ 1.4460.

Found %: C 60.40, 60.78; H 7.98, 8.18. $C_{10}H_{16}O_4$. Calculated %: C 60.00; H 8.00.

Preparation of methylenecyclopentene (V). 100 g of the diacetate (X) was fed dropwise in a stream of nitrogen into a tube filled with pyrex rings (2-mm diameter) at a temperature of 500°. The rate of addition was one drop per second. The pyrolysis products were washed with water and 10% sodium carbonate solution and dried with sodium carbonate. Distillation on a column yielded 18 g of methylenecyclopentene (V) with b.p. 79.5° (750 mm), $n^{17}D$ 1.4850, λ_{max} 234 mμ, ε 14000 (in heptane), and also 3 g of a fraction of monoacetate (XI) with b.p. 74-76° (18 mm), $n^{20}D$ 1.4500. Hydrolysis of this fraction with alcoholic alkali yielded 0.5 g of cyclopentenylmethanol with b.p. 81-90° (50 mm), $n^{20}D$ 1.4856; the phenylurethan had m.p. 66°. Literature data [5]: b.p. 95-96° (6-8 mm), $n^{25}D$ 1.4851; phenylurethan, m.p. 65-67°.

Reaction of cyclohexanone with ketene. Into a very well-stirred mixture of 100 ml of cyclohexanone, 100 ml of ether and 0.5 ml of boron trifluoride etherate at 0-2° was passed ketene (10 g/hour) for four hours. At the end of the reaction, the product was treated with a few milliliters of saturated sodium carbonate solution, dried with magnesium sulfate, filtered carefully and the residue, after removal of the ether, was heated at 110° until the evolution of carbon dioxide ceased. We obtained 20 g of methylenecyclohexane (XV) with b.p. 100-102°, 35 g of cyclohexanone with b.p. 100-102° (150 mm), $n^{20}D$ 1.4500, and also 15 g of a dimer of undetermined structure.

The methylenecyclohexane (XV), obtained from a series of experiments, was dried with potassium carbonate and distilled on a column of 20 theoretical plates. 200 g of a fraction with b.p. 100-108° was taken for distillation and yielded 150 g of pure methylenecyclohexane with b.p. 102.5° (738 mm), $n^{20}D$ 1.4510.

The reaction of cyclohexanone with ketene was studied under various conditions and with various catalysts The results of these experiments are given in the table.

Preparation of Methylenecyclohexane (XV)

Expt. No.	Amount of components	Catalyst	Amt of catalyst	Temperature	Time (hours)	Yield of (XV) (in g)	Starting material recovered (in g)
1	Cyclohexanone 100 ml	BF_3	0.5 ml	−10°	4	10	30
2			0.5 ml	0	2	15	40
3			0.5 ml	−40	2	10	70
4		$HgCl_2$	2 g	0	2	20	50
5			1 g	0	2	25	50
6		H_3BO_3	5 g	28	3	5	90
7		$ZnCl_2$	0.5 g	− 5	2	25	−
8	Cyclohexanone 100 ml + + ether 200 ml	BF_3	1.5 ml	0	2	30	30
9			1.5 ml	8	2	25	30
10			1 ml	0	2	45	30
11			1 ml	0	2	65	10
12			1 ml	0	2	70	10
13		$ZnCl_2$	0.5 g	0	2	30	15

Pyrolysis of diacetate (XVII). The glycol, obtained by oxidation of methylenecyclohexane [8] (XV), was acetylated with a mixture of acetyl chloride and dimethylaniline. We obtained an 86% yield of the diacetate (XVII) with b.p. 137-140° (18 mm), $n^{20}D$ 1.4538.

Found %: C 62.04, 62.02; H 8.71, 8.59. $C_{11}H_{18}O_6$. Calculated %: C 61.68; H 8.41.

110 g of the diacetate (XVII) was fed dropwise in a stream of nitrogen through a tube at 500°, filled with pyrex rings, over a period of two hours. The usual treatment of the reaction products and their distillation on a column yielded 35 g (87%) of methylenecyclohexene.

B.p. 112.5° (750 mm), $n^{20}D$ 1.4930, λ_{max} 231 mμ, ε 15000 (heptane), IR-spectrum determined in CCl_4: 1125, 1425, 1650, 2960 cm^{-1}. Raman spectrum: 1214.4 (int.), 1637 (very int.), 2491.1 (weak), 2873.9 (weak), 3125 (int.), 3339.6 (weak), 3419.6 (average) cm^{-1}.

In addition, we obtained 2 g of acetoxymethyl-Δ'-cyclohexene (XIX) with b.p. 92-96° (16 mm), $n^{20}D$ 1.4450. When hydrolyzed with alcoholic alkali, 1 g of the substance was converted into Δ'-cyclohexenylmethanol (0.5 g) with b.p. 95-97° (20 mm), $n^{20}D$ 1.4915; the phenylurethan had m.p. 95°. Literature data [5]: b.p. 95-96° (23 mm), $n^{20}D$ 1.4905.

Pyrolysis of diacetate (XXII). Glycol (XXI), obtained by oxidation of methylcyclohexene [6, 8], was acetylated by the procedure described above. The diacetate (XXII) obtained (80% yield) had b.p. 132-134° (200 mm), $n^{20}D$ 1.4500.

Found %: C 62.09, 61.68; H 8.36, 8.39. $C_{11}H_{18}O_4$. Calculated %: C 61.8; H 8.41.

110 g of the diacetate was fed dropwise over a period of three hours in a stream of nitrogen through a pyrex tube filled with glass rings at 460°. The pyrolyzate was treated in the usual way to yield 12 g of a mixture of dienes (XVIII) and (XXIII), b.p. 52.5° (105 mm), $n^{20}D$ 1.4820 (λ_{max} 231 and 262 mμ) (fraction A), 25 g of monoacetate (XXIV) with b.p. 96° (30 mm), $n^{20}D$ 1.4590 and 24 g of the starting diacetate (XXII) with b.p. 125-135° (20 mm), $n^{20}D$ 1.4480-1.4520.

5 g of fraction A was heated with maleic anhydride in 15 ml of ethylbenzene at 30° for one hour. The solution of reaction products was washed with warm water and dried with potassium carbonate. Distillation of the hydrocarbon layer on a column of 40 theoretical plates yielded 2 g of methylenecyclohexene (XVIII) with b.p. 52.5° (105 mm), $n^{20}D$ 1.4915, λ_{max} 231.5 mμ. In addition, the aqueous extracts yielded an acid, corresponding to the adduct of 2-methylcyclohexadiene (XXIII) with maleic anhydride. The acid obtained was converted into an anhydride with m.p. 60-61° and through the anhydride into a toluidide with m.p. 180° (literature data [10]: m.p. 62 and 182°). Hydrolysis of (XXIV) gave the corresponding alcohol (30%) with b.p. 70-72° (18 mm), whose phenylurethan melted at 92.5°. Literature data [9]: b.p. 70-72° (16 mm) and phenylurethan, m.p. 94°.

Preparation of pinonic acid (XXV). 60 g of α-pinene was added to a mixture of 1 kg of ice, 1 liter of water and 158 g of permanganate. The mixture was stirred until the permanganate was decolorized and the manganese dioxide was separated and washed with water (twice with 120 ml each time). The filtrate and wash waters were extracted with chloroform (five times with 50-ml portions) and the aqueous layer acidified with 40 ml of concentrated sulfuric acid in 10 ml of water and extracted with chloroform. The residue, after evaporation of the solvent, crystallized. We obtained 38 g of a mixture of racemic and active forms of the acid (XXV) with m.p. 80-90°. Oxidation of (XXV) with sodium hypobromite solution at 0° yielded 70 g of a mixture of pinonic acids (XXVI) with m.p. 100-105°.

Preparation of diamine (XXVIII). With stirring and cooling to 0°, 118 g of the acid chloride of pinonic acid (XXVII) (b.p. 52-54° at 20 mm) in 500 ml of ether was added to a solution of 100 g of sodium azide in 400 ml of water. The mixture was stirred for four hours and the ether layer separated and washed with 5% sodium bicarbonate solution and dried with magnesium sulfate. The dried ether solution was added dropwise to boiling benzene (200 ml), which produced a vigorous evolution of nitrogen. The addition of the solution required five hours. The benzene solution was boiled for one more hour and then the reaction products were added dropwise to 500 ml of boiling hydrochloric acid over a period of four hours. Boiling was continued until the evolution of carbon dioxide ceased. The aqueous solution was evaporated to dryness in vacuum and the free amine liberated with excess 30% sodium hydroxide, dried with solid sodium hydroxide and distilled. We obtained 37 g of diamine (XXVIII) with b.p. 108-110° (40 mm), $n^{20}D$ 1.4750, whose dipicrate had m.p. 252-253° (decomp.).

Found %: N 22.05, 22.16. $C_7H_{16}N_2$. Calculated %: N 21.85.

Methylation of diamine (XXVIII). 37 g of the diamine was added with stirring and cooling to 75 ml of 85% formic acid; 75 ml of 40% formalin solution was added to the mixture, which was then heated at 95-97° for 16 hours. With cooling and stirring, 52 ml of concentrated hydrochloric acid was added to the reaction products. The solution of reaction products was evaporated in vacuum and the residue decomposed with excess 30% sodium

hydroxide. The liberated layer of amine was separated, dried with solid sodium hydroxide and distilled. We obtained 44 g (85%) of tetramethyldiamine (XXIX) with b.p. 110-114° (40 mm), $n^{20}D$ 1.4480.

Found %: N 14.70, 14.80. $C_{11}H_{24}N_2$. Calculated %: N 15.30.

The dipicrate had m.p. 208-210° (decomp.) (from methanol).

Preparation of dimethiodide (XXX). Over a period of three hours, 132 g of methyl iodide was added to 44 g of tetramethyldiamine (XXIX) in 40 ml of methanol with stirring and cooling. The reaction product was left overnight and then boiled under reflux for one hour. The solvent and excess methyl iodide were removed in vacuum and the residual oil crystallized when ground with ether. Recrystallization from a mixture of acetone and methanol yielded 100 g (82%) of the dimethiodide (XXX) with m.p. 228-230° (decomp.).

Found %: N 6.60, 6.40. $C_{13}H_{30}N_2I_2$. Calculated %: N 6.05.

Preparation of 2,2-dimethylmethylenecyclobutene (XXXI). The methiodide (XXX) was converted into the quaternary ammonium base by treatment with moist silver oxide and the base was pyrolyzed at 140° in a vacuum of 40 mm [3]. In this way, 50 g of (XXX) yielded 3 g of 2,2-dimethylmethylenecyclobutene (XXXI) with b.p. 60-63° (730 mm), $n^{20}D$ 1.4275, λ_{max} 229 mμ, ε 7200 (heptane). The diene (XXXI) formed a considerable amount of tar during distillation. Ozonization of the diene yielded formaldehyde (isolated as the dimedone derivative) and dimethylmalonic acid.

Pyrolysis of diacetate (XXXIV). The glycol (XXXIII), prepared by oxidation of 1,2-dimethylcyclohexene [7] in 70% yield, had m.p. 93-94° (from ether).

Found %: C 67.03, 67.26; H 11.16, 11.30. $C_8H_{16}O_2$. Calculated %: C 66.67; H 11.11.

Acetylation of (XXXIII) by the procedure described above, gave a 92% yield of the diacetate (XXXIV) with m.p. 85-86°.

Found %: C 63.24, 63.28; H 8.67, 8.72. $C_{12}H_{20}O_4$. Calculated %: C 63.20; H 8.78.

60 g of diacetate (XXXIV) in 80 ml of acetic acid was pyrolyzed in a stream of nitrogen at 450° over a period of two hours. Working up in the usual way and distillation yielded 10 g of 2-methylmethylenecyclohexene (XXXV) with b.p. 84-87° (150 mm), $n^{20}D$ 1.4860, λ_{max} 235.5 μ, ε 9590 (in heptane).

Found %: C 89.50, 89.80; H 9.80, 10.20. C_8H_{12}. Calculated %: C 89.70; H 10.30.

When oxidized with potassium permanganate in the cold, diene (XXXV) gave glutaric acid in about 65% yield. In contrast to methylenecyclohexene, the diene obtained gave a crystalline adduct with maleic anhydride when the components were heated in a benzene solution at 100° for two hours. The adduct was obtained in about 60% yield and its m.p. was 91-92°.

SUMMARY

1. Two methods of preparing methylenecyclopentene for the first time were developed.

2. A study was made of the condensation of cyclohexanone with ketene and a new method of synthesizing methylenecyclohexene was developed, based on the methylenecyclohexane thus obtained.

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DIENE SYNTHESIS INVOLVING TRANS-α-DIHYDROMUCONIC ACID

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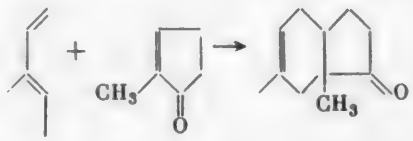
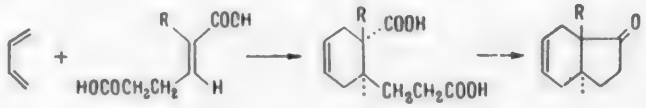
We studied the condensation of α,β-unsaturated cyclic ketones with various cyclic dienes in order to build up various polycyclic systems, including some related to the steroids [1]. In accordance with Alder's rule, this formed compounds containing the cis-indan system.



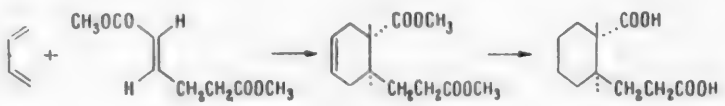
It was not possible to prepare cyclic compounds with trans-coupling of the rings and with the keto group in the position required for a steroid system by this method.

It seemed interesting to condense dienes with α,β-unsaturated dicarboxylic acids of such a structure that the cyclic dicarboxylic acids obtained in this way could be cyclized into the corresponding derivatives of trans-indanone.



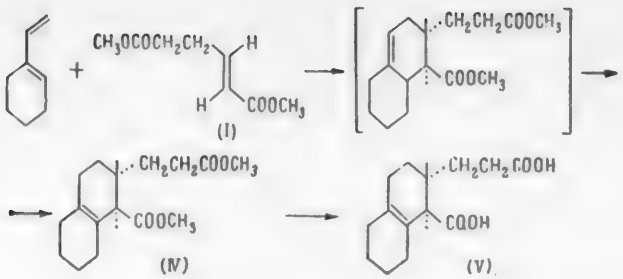
This scheme could replace the complex and multistage means of building up side chains of cyclic o-dicarboxylic acids by the Arndt-Eistert method, which has been used up to now in analogous cases [2].

We were able to condense the dimethyl ester of trans-α-dihydromuconic acid (butene-1-dicarboxylic-1,4 acid, I) with butadiene and 1-vinyl-Δ^1-cyclohexene. In the first case, with the reaction at 210°, we obtained the trans-diester (II), whose structure and configuration was proved by hydrogenation and hydrolysis into the known trans-β-(1-carboxycyclohexyl-2)-propionic acid (III) [3].



(I) (II) (III)

An analogous condensation of diester (I) with vinylcyclohexene led to the bicyclic trans-diester (IV). The latter was not hydrogenated in the presence of palladium on barium sulfate or a platinum catalyst, apparently indicating migration of the double bond into the position between the rings. Hydrolysis of the diester (IV) yielded the corresponding dicarboxylic acid, whose structure was taken as trans-β-(1-carboxy-$\Delta^{9(10)}$-octalyl-2)-propionic acid (V) in analogy with other examples [1].



We also synthesized trans-pentene-2-dicarboxylic-2,5 acid (VI), which is a homolog of dihydromuconic acid, by the following scheme:

$$CH_3CH(COOH)_2 + CHOCH_2CH_2COOCH_3 \rightarrow HOCOC(CH_3)=CHCH_2CH_2COOCH_3$$
$$\rightarrow HOCOC(CH_3)=CHCH_2CH_2COOH$$
(VI)

Attempts to condense it with divinyl at 200° gave no results and the acid was recovered unchanged.

Thus, the presence of a methyl group at the double bond in the position α to the carboxyl hinders the reaction, at least in the presence of a large β-substituent, as in our case. In connection with this, we note that Buchta recently condensed pentene-2-carboxylic-2-acid with 1-vinyl-6-methoxy-3,4-dihydronaphthalene and obtained the expected adduct in only an insignificant yield [4]. Apparently, in this case, the simultaneous presence of a large β-substituent and a CH_3 group in the α-position in the dienophile hindered the reaction.

EXPERIMENTAL

The methyl ester of β-formylpropionic acid was prepared by reducing the acid chloride of succinic half ester by the Rosenmund method and had b.p. 85-87° (20 mm), $n^{20}D$ 1.4256.

Trans-α-dihydromuconic acid was prepared by condensation of the methyl ester of β-formylpropionic acid with malonic acid [5] in the presence of pyridine with subsequent hydrolysis of the intermediate half ester. The yields in the condensation did not exceed 30% as compared with 60% reported previously [5]. When the reaction was carried out in the presence of a small amount of piperidine, the yield could be raised to 44%. Treatment of the acid with diazomethane yielded the dimethyl ester of trans-α-dihydromuconic acid (I) with b.p. 101-104° (2 mm), $n^{20}D$ 1.4522.

Condensation of the dimethyl ester of trans-α-dihydromuconic acid (I) with divinyl. A mixture of 5.5 g of divinyl, 15 ml of benzene and 3.9 g of ester (I) was heated in a steel ampoule at 210° for three hours. Distillation yielded the following fractions: 1st – 30-104° (4 mm), 0.8 g; 2nd – 90-125° (2.5 mm), $n^{17}D$ 1.4554, 2.0 g; 3rd – 125-130° (2.5 mm), $n^{17}D$ 1.4672, 1.9 g; residue ~2 g.

The second fraction was mainly unreacted ester (I) and the third fraction, which appeared as a mobile, yellow liquid, was the dimethyl ester of trans-β-(1-carboxy-Δ^4-cyclohexenyl-2)-propionic acid (II).

1.8 g of the diester (II) in 25 ml of alcohol was hydrogenated over palladium on barium sulfate. After seven hours, the theoretical amount of hydrogen had been absorbed and the hydrogenation stopped. 0.5 g of the hydrogenated diester (without distillation) was hydrolyzed by being stirred with 3 ml of 10% sodium hydroxide at 100° for one hour. When the mixture had cooled, the neutral products were extracted with ether and the aqueous alkali solution acidified with 20% hydrochloric acid and extracted with ether. After evaporation, the extract gave 300 mg of crystals of trans-β-(1-carboxycyclohexyl-2)-propionic acid (III) with m.p. 143-144° (from water). According to the literature data [3], trans-acid (III) melts at 143° and the cis-acid at 103°. The yield, calculated on the ester (I) which reacted, was about 50%.

Found %: C 60.40, 60.20; H 8.30, 8.45. $C_{10}H_{16}O_4$. Calculated %: C 60.00; H 8.10.

Condensation of the dimethyl ester of trans-α-dihydromuconic acid (I) with 1-vinyl-Δ^1-cyclohexene. A mixture of 3.6 g of vinylcyclohexene and 4 g of ester (I) was heated in a glass ampoule at 210° for three hours. Distillation yielded the following fractions: 1st – 20-71° (0.5 mm), $n^{27}D$ 1.4860, 1.6 g; 2nd – 71-150° (0.5 mm), $n^{27}D$ 1.4580, 2.3 g; 3rd – 150-152° (0.5 mm), $n^{27}D$ 1.4926, 1.5 g; residue ~2 g.

The first fraction was mainly unreacted vinylcyclohexene and the second fraction was largely the original ester (I).

The third fraction was the dimethyl ester of trans-β-(1-carboxy-$\Delta^{9(10)}$-octalyl-2)-propionic acid (IV). It was not hydrogenated over either PtO_2, $Pd/BaSO_4$ or Pt on charcoal in alcohol.

1.5 g of diester (IV) was hydrolyzed under the conditions described for the hydrolysis of the diester (II). Acidification yielded a brown oil, which was washed several times with water, the benzene and the water distilled off and the residue left to stand for a long time in a solution in 2 ml of benzene, when it yielded 207 mg of crystals of the acid (V) with m.p. 212-213° (from benzene). The yield, calculated on the ester (I) which reacted, was about 10%.

Found %: C 66.50, 66.70; H 8.10, 8.00. $C_{14}H_{20}O_4$. Calculated %: C 66.65; H 8.00.

The preparation of trans-pentene-2-dicarboxylic-2,5 acid (VI) was carried out similarly to the preparation of trans-α-dihydromuconic acid. To a solution of 11.4 g of methylmalonic acid (15% excess) in 14 ml of pyridine was added 8.2 g of the methyl ester of β-formylpropionic acid and ten drops of piperidine and the solution left for five days. The mixture was then heated for eight hours at 100°, cooled, 16 ml of concentrated hydrochloric acid added and the solution extracted several times with ether. The ether extract was stirred with 250 ml of 10% sodium bicarbonate solution and the aqueous layer separated and acidified with 25 ml concentrated hydrochloric acid. The aqueous layer was extracted, the extract dried with magnesium sulfate and filtered, and the solvent evaporated (finally in vacuum). The solid residue was ground with petroleum ether and filtered off to yield 1.4 g (12.5%) of trans-pentene-2-dicarboxylic-2,5 acid (VI) with m.p. 161-162° (from water).

Found %: C 53.20, 53.00; H 6.50, 6.30. M 164 (by titration with NaOH). $C_7H_{10}O_4$. Calculated %: C 53.20; H 6.40. M 158.

In an attempt to condense acid (VI) with divinyl in dioxane at 200° (four hours), it was recovered unchanged.

SUMMARY

The condensation of the dimethyl ester of trans-α-dihydromuconic acid with divinyl and vinylcyclohexene was accomplished. In the two cases, the corresponding dicarboxylic acids were obtained; the structure of the first of these was proved by hydrogenation into the known trans-β-(1-carboxycyclohexyl-2)-propionic acid.

We also prepared trans-pentene-2-dicarboxylic-2,5 acid, which did not react with divinyl at 200°.

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SYNTHESIS AND CONVERSIONS OF VINYL-α-KETO ALCOHOLS

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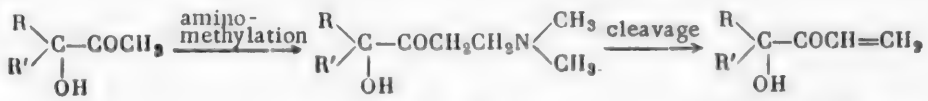
We previously developed a method of preparing various unsaturated α-keto alcohols with a substituted vinyl group by the hydration of acetates of vinylethynylcarbinols and the diacetates of acetylene γ-glycols with subsequent hydrolysis of the unsaturated α-acetoxy ketones [1].

Unsaturated α-keto alcohols are of great synthetic interest due to the presence of functional groups and a double bond, possessing a high activity.

To make a more detailed study of the properties and conversions of unsaturated α-keto alcohols, in the present work we set out to synthesize vinyl-α-keto alcohols. We were able to synthesize unsaturated α-keto alcohols with an unsubstituted vinyl group, starting from tertiary acetylcarbinols, by the following series of conversions.



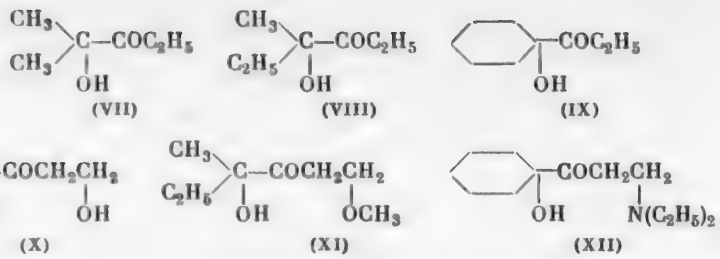
(I) R = R′ = CH_3,
(II) R = CH_3, R′ = C_2H_5,
(III) R, R′ = $(CH_2)_5$,

(IV) R = R′ = CH_3,
(V) R = CH_3, R′ = C_2H_5,
(VI) R, R′ = $(CH_2)_5$.

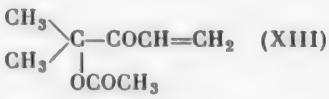
It was found that the Mannich reaction proceeded normally with tertiary acetylcarbinols and led to the formation of β"-amino-α-keto alcohols in yields of about 70%. Thus, heating dimethyl- and methylethylacetylcarbinols and also 1-acetylcyclohexanol with paraformaldehyde and dimethylamine hydrochloride in alcohol solution formed the corresponding β'-dimethylamine-α-keto alcohols (I), (II) and (III). The latter were readily acylated with acid chlorides to form esters, which could be of interest for pharmacological investigations and for the synthesis of physiologically active substances.

The Mannich bases obtained in this way were cleaved in the form of their quaternary ammonium salts. When the ethiodides or the hydrochlorides of the aminoketo alcohols (I), (II) and (III) were heated (140-200°) in vacuum, they formed the corresponding vinyl-α-keto alcohols (IV), (V) and (VI). The vinyl-α-keto alcohols we synthesized were colorless or slightly yellowish liquids with a sharp, lacrimatory smell. In contrast to α-keto alcohols, with a substituted vinyl group, they polymerized on standing for several days at room temperature to give a gel and then changed into a glasslike mass.

When hydrogenated in the presence of a Pt-catalyst, the vinylketo alcohols smoothly absorbed 1 mole of hydrogen and formed the corresponding saturated α-keto alcohols (VII), (VIII) and (IX). Like other unsaturated α-keto alcohols, the vinyl-α-keto alcohols readily added water, alcohols and amines to form β-functionally substituted α-hydroxy ketones. Thus, for example, hydration of vinyl-α-keto alcohol (IV) with dilute sulfuric acid formed ketodiol (X) and the addition of methanol and diethylamine to α-keto alcohols (V) and (VI) yielded the β'-methoxy-α-ketol (XI) and β'-diethylamino-α-ketol (XII), respectively.



The acetylation of vinyl-α-keto alcohol (IV) with acetic anhydride in the presence of traces of sulfuric acid gave the vinyl-α-acetoxy ketone (XIII).



EXPERIMENTAL

The tertiary acetylcarbinols were prepared by hydration of the corresponding ethynylcarbinols under the conditions of the Kucherov reaction [2].

Aminomethylation of dimethylacetylcarbinol. A mixture of 20.4 g of dimethylacetylcarbinol (b.p. 101-103°, $n^{20}D$ 1.4205), 16.3 g of dimethylamine hydrochloride, 10 g of paraformaldehyde and 50 ml of alcohol was boiled under reflux for eight hours. The alcohol was distilled from the homogeneous reaction solution under vacuum and the partly crystalline residue was treated with a saturated aqueous solution of potassium carbonate; the free base liberated was extracted with ether, dried with magnesium sulfate and vacuum distilled. We obtained 23.1 g (72.5%) of dimethyl-β-dimethylaminopropionylcarbinol (I).

B.p. 68-70° (2 mm), 84-85° (8.5 mm), $n^{20}D$ 1.4465, d^{20}_4 0.9532, MR 44.58; calculated 44.62.

Found %: N 8.61, 8.40. $C_8H_{17}O_2N$. Calculated %: N 8.79.

The hydrochloride of the aminoketo alcohol (I) melted at 131.5-133° (from alcohol).

Found %: N 7.30, 6.89. $C_8H_{18}O_2NCl$. Calculated %: N 7.15.

When 1.5 g of the aminoketo alcohol (I) hydrochloride was heated on a water bath with 6 g of acetyl chloride until the evolution of hydrogen chloride ceased and the reaction mixture was subsequently treated with a mixture of ether and alcohol, we obtained 1.1 g of the hydrochloride of the acetate of dimethyl-β-dimethylaminopropionylcarbinol with m.p. 148-149.5°.

Found %: N 5.88, 6.08. $C_{10}H_{20}O_3NCl$. Calculated %: N 5.89.

Aminomethylation of methylethylacetylcarbinol. A mixture of 30 g of methylethylacetylcarbinol (b.p. 149-150°, $n^{20}D$ 1.4200), 22 g of dimethylamine hydrochloride, 13 g of paraformaldehyde and 65 ml of alcohol was boiled for ten hours under reflux. The reaction mixture was treated as described above. We obtained 29 g (65%) of methylethyl-β-dimethylaminopropionylcarbinol (II).

B.p. 76-77° (3 mm), $n^{20}D$ 1.4490, d^{20}_4 0.9521, MR 48.80; calculated 49.20.

Found %: N 8.17, 7.97. $C_9H_{19}O_2N$. Calculated %: N 8.08.

The picrate of the aminoketo alcohol (II) melted at 137.5-139.5° (from alcohol).

Found %: N 13.89, 14.07. $C_{15}H_{22}O_9N_4$. Calculated %: N 13.92.

Aminomethylation of 1-acetylcyclohexanol. A mixture of 35 g of 1-acetylcyclohexanol (b.p. 86-88° at 9 mm, $n^{20}D$ 1.4690), 22 g of dimethylamine hydrochloride, 15 g of paraformaldehyde and 70 ml of alcohol was boiled under reflux for ten hours. After removal of the alcohol in vacuum, the residue was carefully treated with dry acetone and the crystals of hydrochloride (29.5 g) which separated were filtered off. The acetone was distilled from the mother solution, the residue treated with aqueous potassium carbonate solution, and extracted

with ether and a stream of dry hydrogen chloride passed into the ether extract after it had been dried with magnesium sulfate. We obtained, in all, 40.5 g (70%) of the hydrochloride of 1-(β-dimethylaminopropionyl)-cyclohexanol (III) with m.p. 134.5-136.5° (from a mixture of alcohol and acetone).

Found %: N 6.10, 5.95. $C_{11}H_{22}O_2NCl$. Calculated %: N 5.94.

The free base of the aminoketo alcohol (III), liberated by treatment of the hydrochloride (m.p. 134.5-136.5°) with aqueous potassium carbonate solution, melted at 63-65° (from petroleum ether).

Found %: N 6.86, 6.79. $C_{11}H_{21}O_2N$. Calculated %: N 7.03.

Cleavage of dimethyl-β-dimethylaminopropionylcarbinol (I). Into a Claisen flask was placed 11.7 g of the aminoketo alcohol (I) and 0.005 g of pyrogallol and 22 g of ethyl iodide added portionwise. When the evolution of heat had ceased, the reaction mixture was gradually heated on an oil bath in a vacuum of 10-12 mm. Distillation of the cleavage product began at a bath temperature of 135°. After the reaction, the temperature was raised to 200°. As a result of a second distillation (in the presence of pyrogallol) we obtained 5.9 g (70%) of dimethylacrylylcarbinol (IV) in the form of a rapidly polymerizing liquid with a sharp, lacrimatory smell.

B.p. 48-50° (11 mm), $n^{20}D$ 1.4430, d^{20}_4 0.9685, MR 31.24; calculated 30.96.

Found %: C 63.10, 63.03; H 9.01, 8.86. $C_6H_{10}O_2$. Calculated %: C 63.15; H 8.83.

The hydrochloride of the aminoketo alcohol (I) was cleaved similarly.

Acetylation of dimethylacrylylcarbinol (IV). The action of 5 g of acetic anhydride containing a drop of sulfuric acid on 3 g of vinylketo alcohol (IV) proceeded with strong heat evolution and darkening of the reaction mixture. Working up in the usual way yielded 0.5 g of the acetate of dimethylacrylylcarbinol (XIII) with b.p. 69-74° (10 mm). The residue of tarry materials in the flask was 2.6 g.

The 2,4-dinitrophenylhydrazone of the vinyl-α-acetoxy ketone (XIII) melted at 139-141° (from alcohol) and had λ_{max} 347 mμ (in isooctane).

Found %: N 17.01, 16.85. $C_{14}H_{16}O_5N_4$. Calculated %: N 16.66.

Hydrogenation of dimethylacrylylcarbinol (IV). 3 g of substance (IV) was hydrogenated in 15 ml of alcohol in the presence of Pt-catalyst. The theoretical amount of hydrogen required for one double bond was absorbed. We obtained 2.3 g of dimethylpropionylcarbinol (VII) [3] as a colorless liquid with a fruity smell.

B.p. 52-53° (13.5 mm), $n^{20}D$ 1.4225, d^{20}_4 0.9440.

The semicarbazone of dimethylpropionylcarbinol (VII) precipitated as the monohydrate with m.p. 126-130° (from benzene).

Found %: N 22.15, 22.11. $C_7H_{15}O_2N_3 \cdot H_2O$. Calculated %: N 22.00.

Hydration of dimethylacrylylcarbinol (IV). A mixture of 8 g of vinylketo alcohol (IV), 20 g of 15% sulfuric acid and 0.005 g of pyrogallol was stirred vigorously at 50-70° for ten hours. The hydration product was saturated with potassium carbonate, carefully extracted with ether, dried with magnesium sulfate and vacuum distilled. We obtained 1 g of the starting α-keto alcohol (IV) with b.p. 50-51° (11 mm), $n^{20}D$ 1.4410 and 4.1 g of dimethyl-β-hydroxypropionylcarbinol (X) as a thick, colorless liquid.

B.p. 100-102° (3 mm), $n^{20}D$ 1.4545, d^{20}_4 1.0957, MR 32.67; calculated 32.97.

Found %: C 54.13, 54.01; H 9.44, 9.36. $C_6H_{12}O_3$. Calculated %: C 54.55; H 9.09.

The semicarbazone of ketodiol (X) melted at 154-156° (from alcohol).

Found %: N 22.40, 22.56. $C_7H_{13}O_3N_3$. Calculated %: N 22.22.

Cleavage of methylethyl-β-dimethylaminopropionylcarbinol (II). Into a Claisen flask was placed 10 g of aminoketo alcohol (II) and 0.005 g of pyrogallol and 20 g of ethyl iodide was gradually added; the reaction mixture gave off heat and separated into layers. The excess ethyl iodide was distilled off on a water bath. The ethiodide obtained was cleaved at 130-180° in a vacuum of 10-15 mm. Redistillation (in the presence of pyrogallol) of the distillate yielded 6.8 g (92%) of methylethylacrylylcarbinol (V).

B.p. 56-58° (10 mm), $n^{20}D$ 1.4450, d^{20}_4 0.9530, MR 35.81; calculated 35.58.

Found %: C 65.74, 65.32; H 9.74, 9.50. $C_7H_{12}O_2$. Calculated %: C 65.62; H 9.44.

Hydrogenation of methylethylacrylylcarbinol (V). The hydrogenation of 2.7 g of substance (V) in 10 ml of alcohol in the presence of a Pt-catalyst yielded 2.5 g of methylethylpropionylcarbinol (VIII).

B.p. 54-56° (10 mm), $n^{20}D$ 1.4260, d^{20}_4 0.9288, MR 35.92; calculated 36.06.

Found %: C 64.29; H 10.82. $C_7H_{14}O_2$. Calculated %: C 64.57; H 10.83.

The semicarbazone of the α-keto alcohol (VIII) melted at 136-138° (from benzene).

Found %: N 22.83, 22.57. $C_8H_{17}O_2N_3$. Calculated %: N 22.46.

Addition of methanol to methylethylacrylylcarbinol (V). 3 g of vinylketo alcohol (V) was added with cooling to 15 g of methanol containing three drops of sulfuric acid. On the following day, the methanol was removed in vacuum, the residue treated with aqueous potassium carbonate solution and extracted with ether and the extract dried with magnesium sulfate. We obtained 2.8 g of methylethyl-β-methoxypropionylcarbinol (XI).

B.p. 87-89° (10 mm), $n^{20}D$ 1.4360, d^{20}_4 0.9909, MR 42.27; calculated 42.32.

Found %: C 59.68, 59.51; H 10.30, 10.34. $C_8H_{16}O_3$. Calculated %: C 59.97; H 10.06.

The 2,4-dinitrophenylhydrazone of methoxyketo alcohol (XI) melted at 103.5-105.5° (from alcohol).

Found %: N 16.81, 16.63. $C_{14}H_{20}O_6N_4$. Calculated %: N 16.47.

Cleavage of 1-(β-dimethylaminopropionyl)-cyclohexanol (III). 6 g of the aminoketo alcohol (III) hydrochloride was distilled on a metal bath (150-200°) in a vacuum of 3-5 mm. Redistillation (in the presence of pyrogallol) of the distillate collected yielded 3.15 g (80%) of 1-acrylylcyclohexanol (VI).

B.p. 76-78° (4 mm), $n^{20}D$ 1.4870, d^{20}_4 1.0311, MR 43.01; calculated 42.63.

Found %: C 69.69, 70.03; H 9.10, 9.39. $C_9H_{14}O_2$. Calculated %: C 70.09; H 9.15.

Hydrogenation of 1-acrylylcyclohexanol (VI). The hydrogenation of 2.6 g of the unsaturated keto alcohol (VI) in 10 ml of alcohol in the presence of Pt-catalyst yielded 2.2 g of 1-propionylcyclohexanol (IX).

B.p. 98-100° (10 mm), $n^{20}D$ 1.4681, d^{20}_4 1.0121, MR 42.91; calculated 43.09.

Found %: C 69.05, 68.76; H 10.53, 10.54. $C_9H_{16}O_2$. Calculated %: C 69.19; H 10.32.

The semicarbazone of α-keto alcohol (IX) melted at 198-200° (from alcohol).

Found %: N 19.66, 19.75. $C_{10}H_{19}O_2N_3$. Calculated %: N 19.71.

Addition of diethylamine to 1-acrylylcyclohexanol (VI). 0.5 g of diethylamine was added with cooling to 0.5 g of vinylketo alcohol (VI). On the following day the excess diethylamine was removed in vacuum. The residue was diluted with dry ether and hydrogen chloride passed through the ether solution. We obtained 0.4 g of the hydrochloride of 1-(β-diethylaminopropionyl)-cyclohexanol (XII) with m.p. 114.5-116° (from acetone).

Found %: N 5.22, 5.39. $C_{13}H_{26}O_2NCl$. Calculated %: N 5.31.

SUMMARY

1. It was found that the Mannich reaction proceeded normally with tertiary acetylcarbinols and gave good yields of the corresponding β'-amino-α-keto alcohols.

2. It was shown that heating the quaternary ammonium salts of the β'-amino-α-keto alcohols obtained produced cleavage with the formation of high yields of the corresponding vinyl-α-keto alcohols.

3. A study was made of some of the conversions of the vinyl-α-keto alcohols obtained.

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ISOMERIZATION OF DIMETHYLVINYLCARBINOL IN ACID MEDIA

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A method developed in our laboratory makes it possible to prepare in high yield the most varied tertiary acetylene alcohols [1], which are readily hydrogenated selectively to the corresponding vinyl alcohols. We studied the isomerization of one of the simplest tertiary vinyl alcohols, dimethylvinylcarbinol, in acid media.

It was previously found [2] that the isomerization of dimethylvinylcarbinol into prenol (2-methylbuten-2-ol-4) was a reversible process; consequently, if the primary alcohol formed was removed from the sphere of the reaction then the equilibrium was displaced toward the formation of prenol. However, the use of phthalic anhydride and calcium chloride for this purpose gave no result. Similar data were obtained by Krzyzanowski [3] in the isomerization of linalool into geraniol. In the work of Young and Webb [4] it was found that the acetates of the primary alcohols (prenol and geraniol) were stable and isomerized into the corresponding acetates of the tertiary alcohols (dimethylvinylcarbinol and linalool) only under drastic conditions. Consequently, one would expect that binding the prenol in the form of the acetate under acid conditions would lead to almost complete conversion of the tertiary alcohol into the acetate of the primary alcohol. With this aim, we isomerized dimethylvinylcarbinol in acetic acid and studied the effect of various factors on the yield of the primary product.

The isomerization proceeded under the action of mineral acids (H_2SO_4, H_3BO_3, etc.). It was found that increasing the sulfuric acid concentration led to a sharp fall in the yield of prenyl acetate and an increase in the amount of high-boiling products. At an acid concentration of 0.3%, 8% of condensation products were obtained, at a concentration of 0.6%, 19% were obtained and at 1.2% acid, the yield of prenyl acetate had decreased by a factor of 2 and the high-boiling product yield was 27%; at 2.4% H_2SO_4, the yield hardly reached one-fifth of the yield from a control experiment, and the residue represented 41%; if 48% H_2SO_4 was used, then only condensation products (49%) were formed. This agrees with the observations of Favorskii, Lebedeva and Shchukovskaya [5]. p-Toluenesulfonic and α-naphthalenesulfonic acids acted in the same way as sulfuric. Under standard conditions, phosphoric acid did not produce isomerization, although dimethylvinylcarbinol was partially acetylated. An analogous result was obtained by Lennartz [6]. In isomerization in acetic anhydride, sulfuric and phosphoric acids were found to have similar isomerizing actions [7]. Hydrochloric acid led to considerably lower yields of prenyl acetate. If the acetic acid was saturated with dry HCl, then only a mixture of chlorides was obtained and prenyl acetate was not formed at all. At room temperature, boric acid had a certain isomerizing action only in an amount 20 times greater than the amount of sulfuric acid. Perchloric acid produced extensive condensation.

Under the conditions of our experiments on isomerization, the prenyl acetate changed. Thus if, instead of dimethylvinylcarbinol, prenyl acetate was used for the reaction, after 48 hours the mixture had formed a noticeable amount of tar and after 95 hours it was completely impossible to recover the prenyl acetate taken. In the experiments of Young and Webb [4], geranyl acetate was almost 50% condensed after 225 hours at room temperature in the presence of phosphoric acid.

Very small additions of salts affected the prenyl acetate yield. The most active of the salts we investigated was baked copper sulfate and anhydrous zinc chloride (the latter was apparently slightly more active). Other salts [$CuCl_2$, $Cu(CH_3COO)_2$, $Zn(CH_3COO)_2$, $HgSO_4$, $SnCl_2$] did not noticeably change the yield of prenyl

acetate in comparison with experiments without the addition of salts. An exception is $AlCl_3$, which led to a sharp fall in yield (most probably due to water-soluble condensation products such as terpin hydrate, etc., since volatile substances such as isoprene were not detected). Increasing the amount of fused copper sulfate by a factor of 20 sharply reduced the yield of the primary acetate and the amount of condensation products increased considerably.

The addition of water to the reaction mixture lowered the prenyl acetate yield. When the reaction mixture was heated to 100° in the presence of a small amount of water for 1.5 hours, prenyl acetate was not formed at all (43% of condensation products were isolated). Heating at 70° for three hours yielded 10% of prenyl acetate and 34% of residue. Attempts to bind the water, formed during the reaction, by adding excess drying agent or acetic anhydride to the reaction mixture led to a noticeable fall in the yield of the acetate of the primary alcohol. Performing the reaction in acetic anhydride gave better yields than in a mixture of acetic acid and anhydride.

When dimethylvinylcarbinol was heated with water in a metal ampoule at 170-200° for 2.5 hours, we obtained a 20% yield of prenol. Similar results were obtained previously [8] on the isomerization of linalool into geraniol. Boiling a mixture of dimethylvinylcarbinol with water in the presence of boric acid gave only 6-10% of prenol after 13 hours. Under the same conditions, if water was replaced by glycerol (100°, 12 hours) or dioxane (100°, 20 hours) prenol was not formed at all. The same results as obtained if chloroform, ethyl acetate or nitrobenzene were used. When dimethylvinylcarbinol was heated with boric acid in isooctane (88°, 5 hours), the yield of prenol did not exceed 5%. Removal of the water, obtained if the boric esters of the primary alcohol were formed, by azeotropic distillation also gave unsatisfactory results.

The isomerization rate depended strongly on temperature. Even at 35-38° the usual yield of prenyl acetate (~50%) was attained after 4-5 hours, while about a day was required at room temperature (16-18°) and at 0° no prenyl acetate was formed after ten hours. However, at higher temperatures, rapid condensation of the substance began; even after two hours at 100° the yield of prenyl acetate was zero. This was undoubtedly connected with the effect of sulfuric acid since, when it was replaced by boric acid, the reaction mixture could be heated at 100° for more than ten hours without strong tar formation (heating linalool with H_3BO_3 under the same conditions produced rapid condensation).

The isomerization process proceeded quite rapidly. If the yield of a control experiment (95 hours) was taken as 100%, then after only three hours at room temperature the reaction was 20-25% complete, after six hours, 40-50%, and after 24 hours, the yield reached 100%. From this it follows that the prolonged (several days) treatment accepted in works on the study of alcohol isomerization is unnecessary. When the reaction mixture was heated to 100° in the presence of boric acid, the greatest yield (50%) was obtained after four hours and then it fell. The amount of condensation products thus increased from 10 to 17% only, when the time was extended from two to twelve hours.

Test experiments showed that under the chosen standard conditions, replacing the acetic acid by other organic acids did not increase the yield of the corresponding ester of the primary alcohol.

Formic acid produced strong condensation of the reaction components, even in the absence of sulfuric acid. The same results were obtained with propionic acid as with acetic acid. The use of butyric and isobutyric acids led to the formation of a mixture of esters of the primary and tertiary alcohols in a lower total yield than with acetic acid. In this case, increasing the sulfuric acid concentration apparently increased the total yield. When oleic acid was used, a thick, sticky mass was formed.

EXPERIMENTAL

For the experiments, we used the procedure proposed by Lennartz [6] and employed successfully by Oroshnik and Mallory [9] for the isomerization of 1-chloro-2-methyl-2-acetoxybutene-3 into the corresponding primary acetate.

75 ml of chemically pure, twice-frozen, glacial acetic acid was mixed with 0.5 g of concentrated sulfuric acid* (or another acid agent); the required additives were introduced into the mixture followed by 16 g of dimethylvinylcarbinol, dried and distilled on a column (b.p. 98-99°, $n^{20}D$ 1.4182). The mixture was shaken on a

*The addition of concentrated sulfuric acid to a mixture of acetic acid and the tertiary alcohol noticeably reduced the yield of the primary product.

rocker in a sealed vessel at room temperature (usually 95 hours) or heated under reflux and, if necessary, stirred. After the experiment, the mixture was diluted with water and neutralized with sodium carbonate. The upper layer was separated. The aqueous layer was extracted several times with ether. The ether extract was combined with the organic layer, washed with water and dried with magnesium or sodium sulfate.

Preparation of prenyl acetate. a) To a mixture of 75 ml of acetic acid, 0.5 g of conc. H_2SO_4 and 0.5 g of $CuSO_4$ (baked) was added 16 g of dimethylvinylcarbinol and the mixture left for 50 hours at room temperature (16°). Working-up (see above) and distillation yielded 11.8 g (50%) of prenyl acetate with b.p. 42-44° (9 mm), $n^{18}D$ 1.4294. The residue from the distillation was 4 g and there were no other fractions.

b) A mixture of 16 g of dimethylvinylcarbinol, 75 ml of acetic acid and 15 g of H_3BO_3 was stirred at 100° for four hours. The reaction mixture was treated as indicated above. Two distillations yielded 11.9 g (50%) of prenyl acetate with b.p. 44-46° (13 mm), $n^{18}D$ 1.4310. The residue from the distillations weighed 2.1 g.

Preparation of prenyl isobutyrate and butyrate. a) A mixture of 16 g of dimethylvinylcarbinol, 0.5 g of $CuSO_4$, 110 g of isobutyric acid and 1 g of conc. H_2SO_4 was shaken at room temperature for 95 hours. Working-up and two distillations on a column yielded 6.7 g (23%) of prenyl isobutyrate with b.p. 79.2-79.6° (13 mm), $n^{18}D$ 1.4342.

Found %: C 68.67, 68.77; H 10.22, 10.31. $C_9H_{16}O_2$. Calculated %: C 69.19; H 10.26.

Like prenyl butyrate, prenyl isobutyrate was very difficult to purify from traces of the corresponding acid, which is probably due to their very ready hydrolysis.

Exhaustive hydrogenation yielded isoamylisobutyrate with b.p. 168-173°, $n^{20}D$ 1.4092.

b) A similar procedure yielded 10.7 g of prenyl butyrate (37%) with b.p. 54-59° (11 mm), $n^{20}D$ 1.4324. The residue was 1.1 g. In contrast to prenyl isobutyrate, prenyl butyrate was the main reaction product; besides the fraction indicated, we obtained only 2.3 g of a substance with b.p. 84-131° (11 mm). Hydrogenation gave isoamyl butyrate with b.p. 180-181°.

Preparation of prenol. A mixture of 16 g of dimethylvinylcarbinol and 15 g of H_3BO_3 was heated at 100-110° with stirring. The tertiary alcohol gradually distilled off and fresh carbinol was added to the mixture in its place. After five hours, a further 34 ml (27 g) of carbinol had been added. Working-up (see above) yielded 8.1 g of prenol (b.p. 49-54° at 13 mm, $n^{20}D$ 1.4422), 5.8 g of higher-boiling fractions and 3.3 g of residue. Thus, the yield of prenol was 47%, calculated on the dimethylvinylcarbinol which reacted (not allowing for possible dehydration).

Preparation of prenyl phthalate. A mixture of 1 g of prenol, 1.7 g of phthalic anhydride and 7 ml of pyridine was kept at room temperature for 48 hours. The product was washed with dilute acid and water and dried over Na_2SO_4. We obtained 2.2 g (81.5%) of crystals with m.p. 62° (from petroleum ether).

Found %: C 66.63, 66.63; H 5.90, 5.87. $C_{13}H_{14}O_4$. Calculated %: C 66.65; H 6.02.

SUMMARY

A study was made of the isomerization of dimethylvinylcarbinol in various solvents under the action of mineral acids in relation to the acid concentration, temperature, time, and the addition of water and salts.

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SYNTHESIS OF STEROIDAL COMPOUNDS AND RELATED SUBSTANCES

XLVI. Δ^2-CYCLOHEXEN-4-OL-1-ONE ACETATE AND ITS CONDENSATION WITH 1-VINYL-6-METHOXY-3,4-DIHYDRONAPHTHALENE

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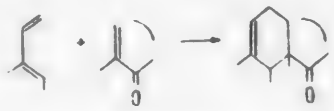
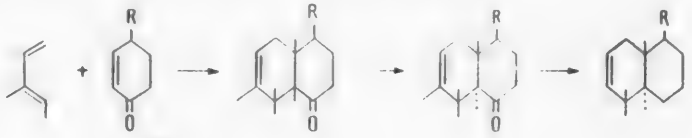
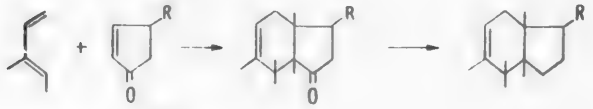
It has been established previously by us [1] that the condensation of α,β-unsaturated cyclic ketones with 1,2-substituted butadienes leads to the formation of only the serial isomers:



Thus, this path permits one to prepare the polycyclic compounds which are related to the steroids, but having the functional substituents in position 15, rather than position 17, which is characteristic for the natural steroids. In order to accomplish the synthesis of compounds which have the necessary substituent in position 17, one may utilize the substituted cyclic ketones of types (A) and (B) for the dienophiles, keeping in mind the subsequent removal of the keto group from the resulting serial isomer.



(A)



(B)

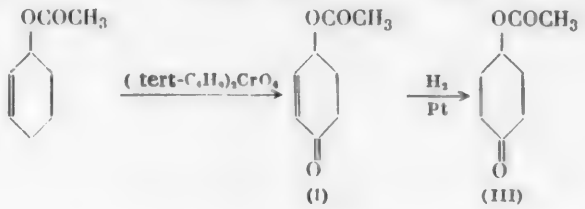
R = OAc, OH, COOH, COOR, CH_2OH, etc.

Ketones of type (A) are of special interest since their condensation products may be readily isomerized into trans-D-homosteroids by the scheme shown above.

In the present paper we describe the synthesis of Δ^2-cyclohexen-4-ol-1-one acetate (I) and its condensation with 1-vinyl-6-methoxy-3,4-dihydronaphthalene (II).

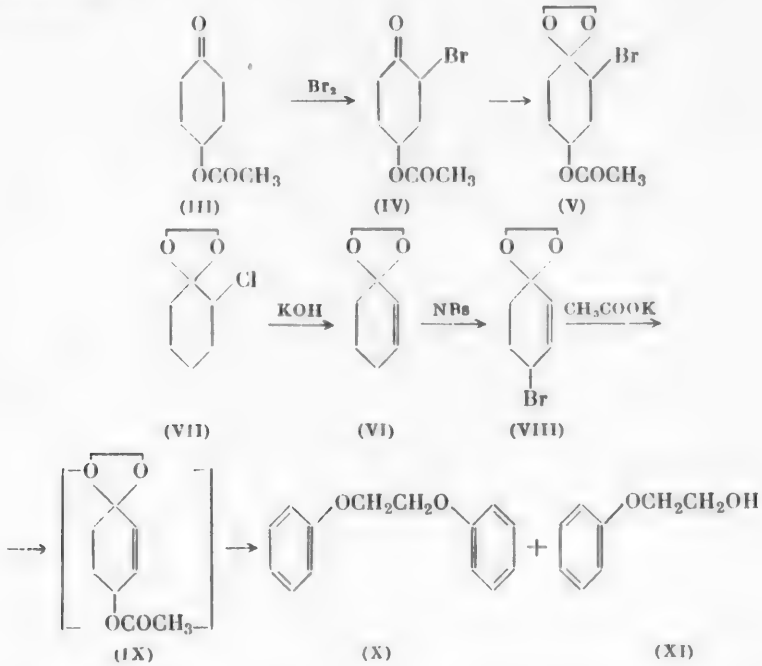
The preparation of ketone (I) presented some considerable difficulties. This was finally accomplished, after a prolonged search, with the synthesis being accomplished by the way of oxidation of Δ^2-hexen-1-ol acetate with tert-butyl chromate in a mixture of carbon tetrachloride and acetic acid. The yield of ketone (I) was

24%, based on the reacted acetoxycyclohexene. The use of chromic anhydride in acetic acid or in pyridine, instead of tert-butyl chromate, or the use of manganese dioxide failed to give the desired result.



The structure of ketone (I) was established by hydrogenation to the known p-hydroxycyclohexanone (III), specially synthesized for this purpose, and by mixed melting point of the corresponding 2,4-dinitrophenylhydrazone specimens.

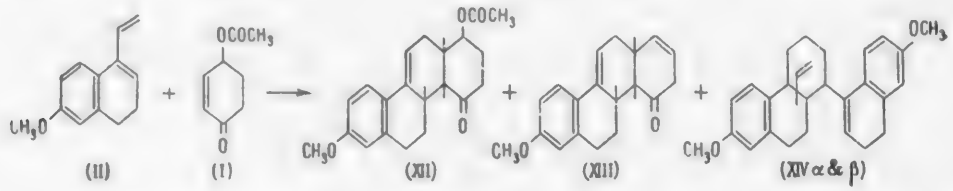
Attempts were made to prepare ketone (I) starting with ketone (III) by the usual technique of bromination-dehydrobromination, used successfully by us in previous work [2]. The bromination reaction proceeded smoothly, but much tar formation occurred when the resulting bromoketone (IV) was heated with diethylaniline at 150° and no individual compounds could be isolated from the reaction products. The same situation was observed also during the dehydrobromination with quinoline. In another variant, the bromoketone (IV) was transformed into the ketal (V), which was treated with sodium tert-butoxide. Here, tar formation was observed again and we could not isolate the desired ketone.



Another scheme for the synthesis of ketone acetate (I) was examined, in which the ketal of Δ^2-1-cyclohexenone was used as the starting material, this being readily prepared from o-chlorocyclohexanone ketal (VII). The ketal (VI) was transformed into the corresponding bromide (VIII) by bromination with N-bromosuccinimide, and this by an exchange reaction with potassium acetate should have yielded, through the intermediate ketal (IX), the desired ketone (I) (after the cleavage of the ketal grouping). The bromination of ketal (VI) proceeded satisfactorily, but during the exchange reaction diphenyl ether of the glycol (X) and monophenyl ether of the glycol (XI) were isolated instead of the expected ketone (I). Both phenyl ethers of glycol were also prepared by a convergent synthesis: ether (X) from ethylene bromide and sodium phenoxide, and ether (XI) from glycol chlorohydrin and sodium phenoxide.

Δ^2-Cyclohexen-4-ol-1-one (I) enters into the Diels-Alder reaction only with some difficulty and is similar,

in this respect, to Δ^2-cyclohexen-1-one. Ketone (I) does not react with 1-vinyl-Δ^1-cyclohexene at 160-170°. It does react at 150-160° with the more reactive 1-vinyl-6-methoxy-3,4-dihydronaphthalene (II) and yields a mixture of products from which we isolated the normal condensation product – 3-methoxy-Δ^9-estrachrysanen-17a-ol-15-one (XII)* in a yield of about 5%, the product of cleavage of acetic acid from the latter – 3-methoxy-$\Delta^{9,17}$-estrachrysadien-15-one (XIII) and two dimers of the original diene (XIV-α and XIV-β).



Dimers (XIV-α) with m.p. 144-146° and (XIV-β) with m.p. 134-135°, differed from each other, evidently, in the location of the double bond and also by exo or endo configurations. Dimer (XIV-β) was also prepared by isomerization of γ-dimer (XIV-γ) with m.p. 169-170°, isolated in insignificant amounts by storage of 1-vinyl-6-methoxy-1-tetrahydrooxonaphthalene and also by its dehydration. Since the isomerization of dimer (XIV-γ) occurs in an acid medium (acetic acid), the double bond in dimer (XIV-β) must be located between the rings.

EXPERIMENTAL

Preparation of Δ^2-cyclohexen-1-ol acetate. Δ^2-Cyclohexen-1-ol acetate was prepared according to Yu.A. Arbuzov's method [4], by oxidation of cyclohexene with selenous acid in acetic acid. The yield, in our experience, failed to go over 15%, as against 33-36%, disclosed by the above author (in the paper the yield is erroneously given as 48-52%). The yield rises to 20% if the reaction mixture is poured with stirring into five parts of cold water after the oxidation, then extracted with ether and vacuum distilled. The resulting acetoxycyclohexene had b.p. 63° (10 mm), and $n^{20}D$ 1.4585.

Preparation of Δ^2-cyclohexen-4-ol-1-one acetate (I). A solution of tert-butyl chromate was prepared by the addition of chromic anhydride to tert-butyl alcohol at 25°, according to the known method [5]. 430 ml of a solution of tert-butyl chromate in carbon tetrachloride (the solution corresponded to 27.5 g of chromic anhydride) was added with stirring to a solution of 20 g of Δ^2-cyclohexen-1-ol acetate in 30 ml of carbon tetrachloride, 100 ml of acetic acid and 40 ml of acetic anhydride, and the mixture was refluxed with stirring for ten hours. After the solvent had been distilled off under a slight vacuum at 50°, crystalline oxalic acid was added, with stirring and ice cooling, to the deep-green viscous solution until the test for Cr^{VI} became negative (about 10 g required), the whole was stirred for one hour longer, the volatiles were distilled off at 70-80° under 30-40 mm vacuum and the residue was extracted repeatedly with chloroform. The chloroform solution was filtered, the chloroform was distilled from it under a slight vacuum and the residue was distilled.

1st fraction – 70-75° (15 mm), 5.2 g; 2nd – 75° (15 mm) and 94° (4 mm), 0.6 g; 3rd – 94-98° (4 mm), $n^{20}D$ 1.4820, 4.1 g; residue – 5 g.

The first fraction consisted mainly of unreacted acetoxycyclohexene. The third fraction was Δ^2-cyclohexen-4-ol-1-one (I).

Pure ketone (I) is a yellowish liquid.

B.p. 71° (2 mm), $n^{20}D$ 1.4845, d^{20}_4 1.1233; MR 39.3; calculated 37.4.

Found %: C 62.30, 62.10; H 6.80, 6.85. $C_8H_{10}O_2$. Calculated %: C 62.30; H 6.50.

The semicarbazone had m.p. 193-196° (from alcohol + dioxane). The 2,4-dinitrophenylhydrazone – orange crystals (from alcohol + dioxane) with m.p. 182-184° (after placement in a bath preheated to 120° and with rapid heating).

λ_{max} (in heptane) 254 mμ (lgε 4.16) and 357 mμ (lgε 4.47).

*Nomenclature in accordance with L.N. Nazarov [3].

For dinitrophenylhydrazones of cyclohexenones [6] the average λ_{max} is 362 mμ and lgε 4.30-4.39.

Hydrogenation of Δ^2-cyclohexen-4-ol-1-one acetate (I). 0.4 g of the acetate in 4 ml of ethyl acetate was hydrogenated over platinum oxide according to Adams. The hydrogenation proceeded very rapidly and, in 20 minutes, 1.5 mole of hydrogen was absorbed.(90 ml instead of 60 ml). Then the hydrogenation became slower, but did not cease. The solution was filtered, evaporated in vacuum at 50°, and the residue was mixed with a solution of 0.15 g of dinitrophenylhydrazine in 10 ml of alcohol. Immediately a precipitate of yellow crystals of the dinitrophenylhydrazone (0.25 g) formed. This melted at 183-183.5°, after recrystallization from alcohol, and gave no depression in a mixed melting point with a sample of the dinitrophenylhydrazone of p-acetoxycyclohexanone prepared below.

Preparation of p-acetoxycyclohexanone (III). p-Benzoxycyclohexanone (m.p. 64-65°) was prepared according to Jones' method [7], starting with quinitol, by a successive benzoylation and oxidation with the over-all yield of 25%.

A mixture of 48 g of p-benzoxycyclohexanone and sodium methoxide solution (from 0.5 g of sodium) in 190 ml of dry methanol was refluxed for 12 hours. 12 ml of water was added to the solution, carbon dioxide was introduced for the neutralization and methanol was distilled off under a slight vacuum. The dark liquid was twice extracted with ether (10-ml portions) to remove methyl benzoate, and the aqueous solution was evaporated under vacuum at 60°. 20 ml of acetic anhydride and 15 ml of dry pyridine were added to the residue and this was heated for 1.5 hours at 100°. 15.0 g (48%) of p-acetoxycyclohexanone (III) was obtained after a distillation (b.p. 103-104° at 7 mm, $n^{20}D$ 1.4600). The dinitrophenylhydrazone had m.p. 182-183° [8].

Bromination of p-acetoxycyclohexanone (III) and an attempt to dehydrobrominate the corresponding bromide (IV). A solution of 9.5 g of bromine in 10 ml of acetic acid was added with stirring over 20 minutes to a solution of 9.7 g of p-acetoxycyclohexanone in 12 ml of acetic acid, taking care that the temperature remained in the interval of 25-28°. After stirring one hour, 100 ml of water was added and the whole was extracted with ether. The extract was dried over sodium sulfate, ether and acetic acid were distilled off under vacuum, the residue (12.5 g) was mixed with 12 g of diethylaniline and heated to 150° (the reaction fails to proceed at 100°) in a nitrogen atmosphere for three hours. The hydrobromide of diethylaniline precipitated after dilution with benzene (6.3 g or 44%). The benzene solution was shaken three times with 20% hydrochloric acid (5 ml each time), filtered, the solvent distilled off and the residue distilled under vacuum. 1.2 g of a liquid with b.p. 80-115° (2 mm) and $n^{20}D$ from 1.50 to 1.52 was isolated, this giving a positive Beilstein test. No individual substance could be isolated from this mixture. Similar results were obtained after the replacement of diethylaniline with quinoline.

Preparation of 2-bromo-4-acetoxy-1-cyclohexanone ketal (V) and its dehydrobromination. A mixture of 17 g of unpurified bromide (IV), prepared above, 50 ml of benzene, 5 g of glycol and 0.1 g of p-toluenesulfonic acid was refluxed with stirring with a water separator trap for three hours, whereupon 1.2 ml of water separated instead of the theoretically expected 1.3 ml. The benzene solution was neutralized by shaking with sodium carbonate solution, dried over magnesium sulfate and the residue distilled twice under vacuum. 8.7 g (44%) of 2-bromo-4-acetoxy-1-cyclohexanone ketal (V) was isolated.

B.p. 107-114° (0.5 mm), $n^{20}D$ 1.5070.

Found %: Br 29.15, 29.05. $C_{10}H_{15}O_4Br$. Calculated %: Br 28.70.

8.5 g of ketal (A) was mixed with sodium tert-butoxide solution (from 4 g of sodium and 60 ml of tert-butyl alcohol), whereupon the mixture became very hot and turned dark. The reaction mixture was refluxed for 14 hours, the tert-butyl alcohol was distilled off under a vacuum, 20 ml of acetic acid and 10 ml of acetic anhydride was added to the residue and the mixture was heated for two hours at 100° (for the removal of the ketal group and for acetylation). The mixture was diluted with 200 ml of ether after having been cooled; the whole was filtered, the solvents and the acid were distilled off under vacuum and the residue was distilled. 0.2 g of a distillate with b.p. 85-87° (3 mm) and $n^{18}D$ 1.4780 was isolated; the semicarbazone could not be isolated from this product.

Bromination of cyclohexenone ketal (VI) with N-bromosuccinimide. The cyclohexenone ketal was prepared by the previously described method [9] and had b.p. 68-69° (10 mm), $n^{17}D$ 1.4800.

24.5 g of pure N-bromosuccinimide was added to the solution of 18 g of the ketal (VI) in 180 ml of dry carbon tetrachloride and the suspension was stirred for 75 minutes at 71-72°. Almost all N-bromosuccinimide was transformed into succinimide during this interval. The temperature should not be raised above 74° since an intense loss of hydrogen bromide occurs otherwise. The mixture was cooled, the precipitated succinimide (14 g) was filtered off, 20 g of dry potassium acetate was added to the filtrate and the carbon tetrachloride was distilled off under a slight vacuum. 40 ml of dioxane was added to the residue and heated for 3.5 hours at 80°. After having been cooled, the reaction mixture was diluted with ether, the mixture of salts was separated, and the precipitate was washed with cold ether. The filtrate was evaporated under vacuum at 40-50°; thereupon, crystals precipitated (2.8 g), having m.p. 83-85°, which were separated and washed with alcohol. The following fractions were isolated during the distillation of the filtrate: 1st – up to 79° (2 mm), $n^{20}D$ 1.5162, 2.4 g; 2nd – 79-85° (2 mm), $n^{20}D$ 1.5338, 4.1 g; 3rd – 85-108° (2 mm), $n^{20}D$ 1.5400, 0.9 g; residue – 3.7 g.

An additional 2 g of crystals with m.p. 83-85° was isolated after the recrystallization of the residue from alcohol. The crystalline substance was diphenyl glycol ether (X). Its yield was 30-35% in the several experiments. It melted at 92-94° after purification (repeated recrystallization from alcohol) and gave no depression with a sample obtained by the reaction of sodium phenoxide with ethylene bromide [10].

The dinitro derivative (evidently di-p-nitrophenyl glycol ether) with m.p. 164-166° (from alcohol + ethyl acetate) was obtained by nitration with cooling in acetic anhydride.

Found %: C 54.90, 55.00; H 4.10, 4.10; N 9.50, 9.40. $C_{14}H_{12}O_6N_2$. Calculated %: C 55.25; H 3.95; N 9.20.

As to the liquid fractions, several experiments were run for a detailed study of these. 52 g of a distillate with b.p. 75-100° (2 mm) was obtained from 126 g of cyclohexenone ketal, this distillate being then subjected to a repeated fractionation. As a result 18.5 g of a substance with b.p. 72-73° (1.5 mm) and $n^{25}D$ 1.5304, was isolated. The substance contained about 1% of bromine owing to admixture of bromides which were not separable by a distillation; however, the product gave an analysis which corresponded to monophenyl glycol ether acetate.

Found %: C 67.80, 67.80; H 7.20, 7.00. $C_{10}H_{12}O_3$. Calculated %: C 67.60; H 6.80.

The remaining fractions contained the unreacted cyclohexenone ketal and higher boiling, bromine-containing products.

Hydrolysis of 4.8 g of the substance by refluxing for three hours with a solution of 3 g of potassium hydroxide solution in 30 ml of alcohol gave, after the usual treatment, 2.6 g of monophenyl glycol ether (XI) with b.p. 90-91° (2 mm), $n^{20}D$ 1.5332.

According to the literature data [11]: b.p. 134-135° (18 mm), $n^{20}D$ 1.5340.

The benzoate, m.p. 59° (from petroleum ether), was obtained by benzoylation of the ether with benzoyl chloride in pyridine. 3,5-Dinitrobenzoate with m.p. 106-108° (from benzene) was prepared in a similar manner.

Found %: N 8.70. $C_{15}H_{12}O_7N_2$. Calculated %: N 8.45.

Preparation of monophenyl glycol ether (XI). 10.9 g of phenol, then 10 g of ethylene chlorohydrin, were added to a solution of sodium ethoxide in alcohol (from 2.82 g of sodium and 50 ml of anhydrous alcohol), and the mixture was refluxed for 12 hours. The alcohol was distilled off, the mixture was diluted with water and extracted with ether. The ethereal solution was washed several times with water, the ether was distilled off and the residue was vacuum distilled. 5.5 g of monophenyl glycol ether with b.p. 118-121° (12 mm), $n^{20}D$ 1.5360, was obtained.

Its benzoate had m.p. 60°; dinitrobenzoate – 103-104°. The respective mixed melting points, with specimens described above, showed no depression.

Condensation of Δ^2-cyclohexen-4-ol-1-one acetate with 1-vinyl-6-methoxy-3,4-dihydronaphthalene (II). 1-Vinyl-6-methoxy-3,4-dihydronaphthalene (II) was prepared according to the method previously described by us [12] and had b.p. 110-112° (1 mm), $n^{20}D$ 1.5935.

A mixture of 5.7 g of 1-vinyl-6-methoxy-3,4-dihydronaphthalene and 4.9 g of acetate (I) were heated in 10 ml of xylene in a sealed ampoule under nitrogen atmosphere for seven hours at 160°. The cherry-colored solution was evaporated under vacuum, diluted with 3 ml of benzene and 3 ml of petroleum ether and set aside

in the cold. 1.25 g of a crystalline mixture precipitated, with 1.55 g additional coming from the mother liquor after evaporation, for a total of 2.8 g. 410 milligrams of 3-methoxy-Δ^9-estrachrysanen-17a-ol-15-one acetate (XII) with m.p. 188-190° was isolated by a successive recrystallization from methanol and benzene.

Found %: C 74.00, 74.15; H 7.15, 7.20. $C_{21}H_{24}O_4$. Calculated %: C 74.10; H 7.10.

180 milligrams of α-dimer (XIV-α) with m.p. 144-146° was also isolated.

Found %: C 83.45, 83.50; H 7.60, 7.40. $C_{26}H_{28}O_2$. Calculated %: C 83.85; H 7.55.

In addition, 40 milligrams of β-dimer (XIV-β) with m.p. 134-135°, was obtained.

Found %: C 83.70, 83.90; H 7.70, 7.70. $C_{26}H_{28}O_2$. Calculated %: C 83.85; H 7.55.

About 5% of the acetoxyketone (XII) was isolated in one experiment and along with it an almost equal amount of 3-methoxy-$\Delta^{9,17}$-estrachrysadien-15-one (XIII) with m.p. 155-157°.

Found %: C 81.10, 81.10; H 7.20, 7.40. $C_{19}H_{20}O_2$. Calculated %: C 81.40; H 7.20.

Isolation of γ-dimer (XIV-γ) and its isomerization into β-dimer (XIV-β). After a dehydration of 10 g of 1-vinyl-6-methoxy-1-tetralol by heating with sand [12] and a subsequent dilution of the reaction mixture with ether, crystals (0.15 g) precipitated, these melting at 169-170°, after a recrystallization from a mixture of methanol and benzene.

Found %: C 83.50, 83.30; H 7.60, 7.60. $C_{26}H_{28}O_2$. Calculated %: C 83.85; H 7.55.

A solution of 130 milligrams of the γ-dimer (XIV-γ) in 3 ml of acetic acid was refluxed for one hour. After a vacuum evaporation and crystallization from a mixture of methanol and benzene, we obtained 35 milligrams of the β-dimer with m.p. 126-128°. A second recrystallization raised the m.p. to 134-135°. A mixed melting point with the specimen isolated above showed no depression.

SUMMARY

Δ^2-Cyclohexen-4-ol-1-one acetate was prepared by oxidation of Δ^2-cyclohexen-1-ol acetate with tert-butyl chromate. Its condensation with 1-vinyl-6-methoxy-3,4-dihydronaphthalene was accomplished, whereby the 3-methoxy-Δ^9-estrachrysen-17a-ol-15-one acetate, 3-methoxy-$\Delta^{9,17}$-estrachrysadien-15-one and two dimers of the original diene were isolated, from the reaction products.

It was possible to isolate only the phenyl and the diphenyl glycol ethers in an attempt to prepare Δ^2-cyclohexen-4-ol-1-one acetate by bromination of Δ^2-cyclohexen-1-one ketal with N-bromosuccinimide with a subsequent treatment with potassium acetate and acetic acid.

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STUDIES IN THE FIELD OF STEREOCHEMISTRY OF CYCLIC COMPOUNDS

XXVIII. CONDENSATION OF 1-ACETOXYBUTADIENE WITH CITRACONIC ANHYDRIDE AND THE STEREOSPECIFIC TRANSFORMATIONS OF THE RESULTING ISOMERIC ADDUCTS

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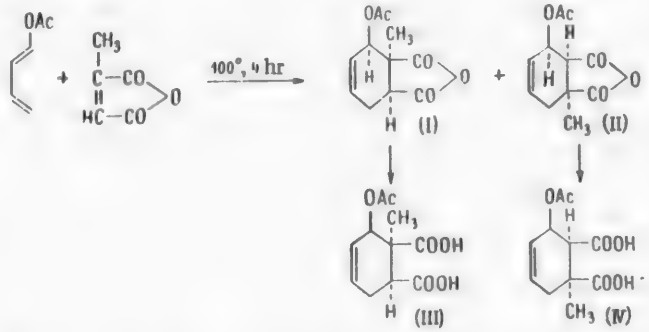
Continuing the previously begun work on the diene reactions with participation of methoxydienes [1] and on the stereochemistry of 3-hydroxycyclohexane-1,2-dicarboxylic acids [2], we examined the condensation of 1-acetoxybutadiene with citraconic anhydride, which is of interest in the study of problems of structural directivity of the Diels-Alder synthesis and the stereochemistry of isomeric adducts. It appeared that, in this condensation, owing to the unsymmetric character of both reacting components, a mixture of approximately equal amounts of both possible ortho and meta adducts (I) and (II) is formed under comparatively mild conditions and in good yield, with the isomeric 2-methyl-3-acetoxy- and 1-methyl-3-acetoxy-Δ^4-cyclohexene-1,2-dicarboxylic acids (III) and (IV) being obtained by hydrolysis of these products with water.

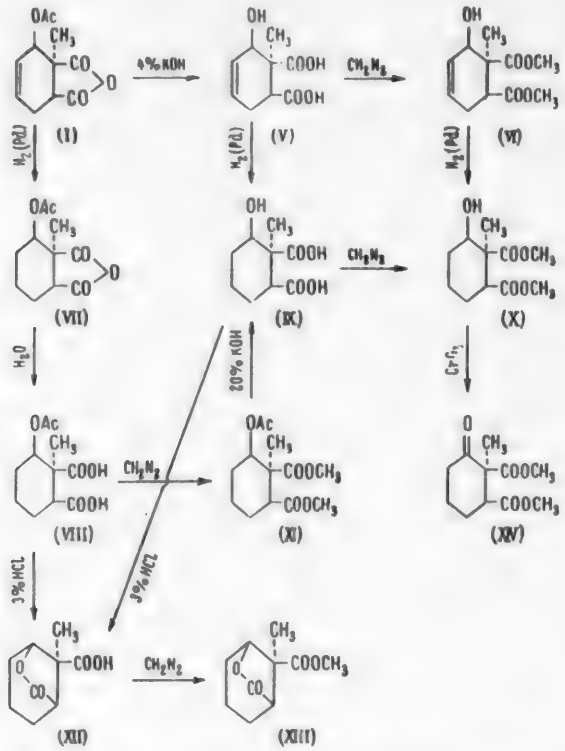


Both isomeric adducts have the cis-cis configuration which corresponds to the reaction course in accord with the Alder rule and, therefore, the presence of the acetoxy group in the acyclic diene does not affect the spatial directivity of the Diels-Alder synthesis to such a degree, as was noted previously, in the case of 1-α-acetoxyvinyl-Δ^1-cyclohexene [3]. The fact of formation of a large amount of the meta isomer in the condensation of 1-acetoxybutadiene with citraconic anhydride indicates, simultaneously, that the electrostatic effect of the acetoxy group is more pronounced for the structural directivity of the Diels-Alder reaction than is the effect of the steric factors which are determined by the volume of the substituents [4].

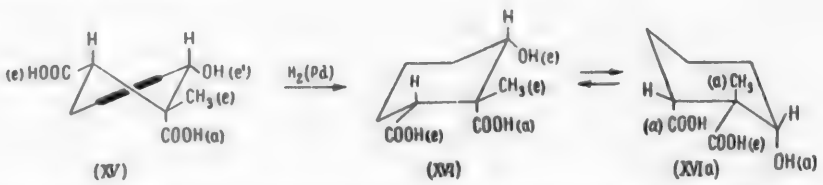
Some of the chemical transformations of the resulting adducts (I) and (II) were studied for the proof of structure and configuration of the latter. In agreement with its structure, the cis-ortho adduct (I) turned out to be thermally stable and yielded Δ^4-hydroxy acid (V) in alkaline hydrolysis, this acid not forming a lactone in the process of formation and yielding the hydroxy diester with diazomethane (VI). The saturated cis-acetoxy anhydride (VII), incapable of cleaving the acetoxy group on heating and hydrolyzable with water to the acetoxy acid (VIII), was obtained quantitatively in the catalytic hydrogenation of the cis-ortho anhydride (I). The 2-methyl-3-hydroxycyclohexane-1,2-dicarboxylic acid (IX) and its diester (X), which correspond to these substances,

were also formed during the catalytic hydrogenation of the corresponding unsaturated hydroxy acid (V) and its diester (VI). The hydroxy acid (IX) is sufficiently thermally stable, is incapable of lactonizing in neutral and alkaline conditions and may be prepared even by the hydrolysis of the saturated acetoxy diester (XI) with 20% aqueous potassium hydroxide solution.

However, during an acidic hydrolysis of the acetoxy acid (VIII) or in a brief heating of the hydroxy acid (IX) with 3% hydrochloric acid, the γ-lacto acid (XII) is formed quantitatively and can be characterized in the form of the crystalline γ-lacto ester (XIII). This transformation proves the cis-cis configuration of the original acetoxy anhydride (I) since only in this case is it possible for the saturated hydroxy acid (IX) to be able to lactonize, owing to the cis disposition of the carboxy group at C_1 and of the hydroxyl at C_3. It follows also, from the fact that the acetoxy acids (III) and (VIII) do not cleave acetic acid during an alkaline hydrolysis with formation of the corresponding unsaturated compounds, that these acids contain the methyl group at C_2 position. This was confirmed additionally by the fact that the hydroxy diester (X), on being oxidized with chromic anhydride in acetic acid, gave the keto diester (XIV) which is incapable of enolizing, the latter being formed in a good yield.



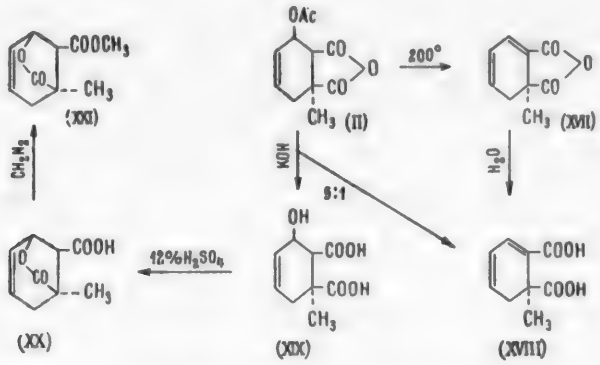
An examination of the molecular models permits us to draw some conclusions about the conformation of all the derivatives of this series and to explain the peculiarities of their lactonization. In accordance with the cis principle of the Diels-Alder synthesis, and with the rule of the maximum number of equatorial substituents, the unsaturated hydroxy acid (V) should have the conformation (XV) in which it would be sufficiently resistant to the intramolecular lactonization.



The saturated hydroxy acid (IX), formed by catalytic hydrogenation, should also correspond to the more stable conformational formula (XVI) by which it is possible to explain its relatively low tendency to lactonize,

despite the cis and meta disposition of the carboxyl and the hydroxyl groups. This acid is capable of lactonization only under acidic conditions and, as it is easy to see, the formation of the lacto acid during this must be realized by means of the conversional form (XVIa). Such an energetically unfavorable transformation of three equatorial substituents to axial ones is apparently compensated by the gain of energy in the lactonization reaction itself, owing to which the formation of the γ-lacto acid occurs (XII).

In contrast to the cis-ortho adduct (I) considered above, the isomeric cis-meta anhydride (II) turned out to be unstable to heat. It readily loses acetic acid, with formation of the unsaturated anhydride (XVII) even at 200° and hydrolysis of the latter product yields 1-methyl-$\Delta^{2,4}$-cyclohexadiene-1,2-dicarboxylic acid (XVIII). This acid has an absorption maximum at 285 mμ, which indicates the presence of a conjugated double-bond system in it, this system being capable of being formed only with the meta structure of the adduct (II). A partial loss of acetic acid also takes place in the alkaline hydrolysis of the cis-meta anhydride (II) and, in this case, there is formed a mixture (in proportions of about 5:1) of Δ^4-3-hydroxy dicarboxylic acid (XIX) and the above-described cyclohexanedienoic acid (XVIII).



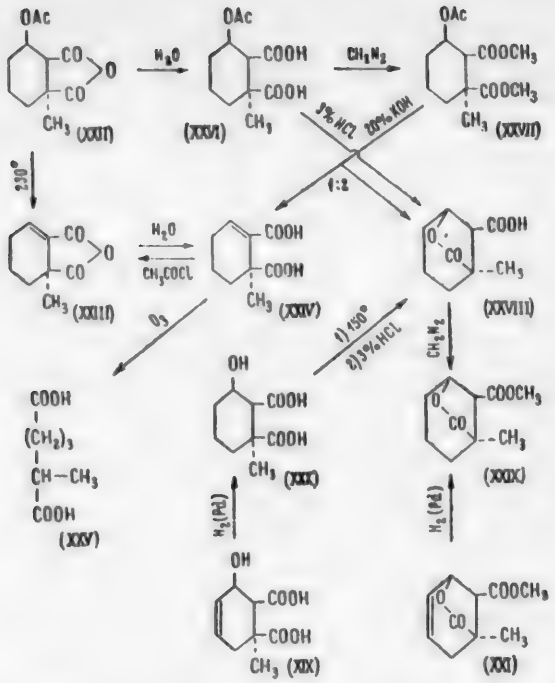
In contrast to the above-described ortho isomer (V), the unsaturated hydroxy acid (XIX) is capable of lactonization and, on being heated with 12% sulfuric acid, yields the unsaturated γ-lacto acid (XX), characterized in the form of the crystalline γ-lacto ester (XXI), which proves, simultaneously, the configuration of the original meta adduct (II).

Similar rules of the reactions of loss of acetic acid and lactonization occur also among the saturated compounds of the meta series. It turned out that the saturated acetoxy anhydride (XXII), obtained by the catalytic hydrogenation of the cis-meta adduct (II), readily loses acetic acid on being heated (as a result of trans-elimination reaction) and is transformed into the unsaturated anhydride (XXIII), which yields 1-methyl-Δ^2-cyclohexene-1,2-dicarboxylic acid (XXIV) on hydrolysis.

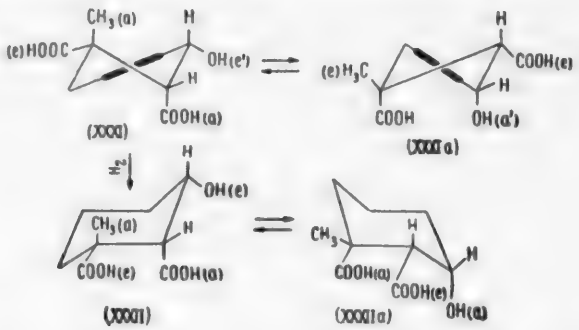
α-Methyladipic acid (XXV) was obtained by ozonization of the unsaturated acid (XXIV), the product being characterized in the form of its diamide with m.p. 185-186° which alone proves the position of the double bond in acid (XXIV), and confirms the structure of the original cis-meta adduct (II).

The acid and the alkaline hydrolyses of acetoxy acid (XXVI) and of its diester (XXVII) were studied for the comparison of the relative ease of cleavage and lactonization of derivatives of the ortho and the meta series. It turned out that lactonization occurs quantitatively and the corresponding γ-lacto acid (XXVIII), whose ester (XXIX) is also obtained by the catalytic hydrogenation of the unsaturated γ-lacto ester (XXI), is formed by heating the acetoxy acid (XXVI) with 5% hydrochloric acid as it occurs, as well, in the isomer of the ortho series (VIII). However, in contrast to the isomer of the ortho series, the lactonization, in this case, occurs considerably more easily since 1-methyl-3-hydroxycyclohexane-1,2-dicarboxylic acid (XXX), formed by hydrogenation of the corresponding unsaturated hydroxy acid (XIX), is completely converted into the above-described γ-lacto acid (XXVIII) at 120-150°.

A still greater difference in the isomer stability occurs in the alkaline hydrolysis. While the ortho acetoxy diester (XI) yields only the hydroxy acid (IX) during such a hydrolysis, boiling meta acetoxy diester (XXVII) with 20% potassium hydroxide solution leads to a mixture of unsaturated dicarboxylic acid (XXIV) and γ-lacto acid (XXVIII) in 1:2 ratio.



All these peculiarities of behavior of the derivatives of the meta series, displayed in the ease of reactions of loss of elements of acetic acid and lactonization, may be explained by examination of the molecular models.



The unsaturated hydroxy acid (XIX), in accord with its cis-cis configuration, should correspond to the more stable conformational formula (XXXI), which does not have a meta axial interaction of the substituents. Having an equal number of axial and equatorial substituents, such a conformation should be more prone (relative to the corresponding ortho isomer) to a transformation into the conversional form (XXXIa) by means of which it lactonizes more readily than does the isomeric hydroxy acid (V). This also explains the ease of lactonization of the saturated hydroxy acid (XXX), whose configuration should correspond to the conformational form (XXXII). In this case, the transformation into the conversional form (XXXIIa), capable of lactonization, does not require a large expenditure of energy, as a result of which fact the lactonization may be realized even after an insignificant heating.

EXPERIMENTAL

Condensation of 1-acetoxybutadiene with citraconic anhydride. 10 g of citraconic anhydride, 50 ml of acetone and 0.1 g of Methylene blue were added to 85 ml of a mixture of 1-acetoxybutadiene with acetic anhydride [2]; the solution was heated in a steel ampoule for four hours at 100-110°. The solvents and the volatile products were distilled off on a steam bath under water-pump vacuum and the liquid residue was dissolved in 15 ml of ethyl acetate. The separated crystalline product was filtered off after an hour of standing at 0° temperature, washed with a small amount of ethyl acetate and yielded 3.5 g of cis-meta anhydride (II) with m.p. 122-125°, which had m.p. 127-128° after a recrystallization from ethyl acetate.

Found %: C 59.10, 59.02; H 5.31, 5.42. $C_{11}H_{12}O_5$. Calculated %: C 58.92; H 5.39.

0.3 g of the cis-meta anhydride (II) was boiled for hydrolysis with 1 ml of water; on cooling, 0.25 g of 1-methyl-3-acetoxy-Δ^4-cyclohexene-1,2-dicarboxylic acid (IV) was isolated, this melting at 174-175° (decomp.) after repeated crystallization from water.

Found %: C 54.61, 54.43; H 5.89, 5.88. $C_{11}H_{14}O_5$. Calculated %: C 54.54; H 5.82.

The mother liquor after the isolation of meta anhydride (II) was evaporated at water-pump vacuum, all admixtures were distilled up to 125-130° at 5 mm from the liquid reaction product and the residue was extracted three times with boiling ether (50 ml each portion). After the ether had been distilled, the resulting product was dissolved by heating with 2 ml of ethyl acetate, 6 ml of ether was added and the solution was left overnight at 0°. The separated crystals were filtered off, washed with ether and yielded 5.1 g of a mixture of ortho and meta anhydrides (I) and (II) with m.p. 82-92°. 1.7 g more of the same mixture with m.p. 81-89° was isolated from the mother liquor after a distillation of the solvents under vacuum, solution of the residue in 5 ml of ether and freezing-out at 0°. For separation of this mixture, the latter was dissolved in 4 ml of ethyl acetate and was allowed to crystallize slowly at room temperature. After the separation of well-formed, platelike crystals had been completed, and needlelike crystals began to appear, the mother liquor was separated and the crystalline residue was washed with ether. 3.1 g of a substance with m.p. 92-95° was isolated, this being mainly the ortho anhydride (I). 0.5 g of needlelike crystals with m.p. 121-125°, which represented the almost pure meta isomer (II), was isolated from the mother liquor on continued standing. A further 1.7 g of the ortho anhydride (I) with m.p. 95-97° and 0.15 g of meta anhydride (II) with m.p. 121-124° may be isolated by repeated fractional crystallization of the residue. The cis-ortho anhydride (I) is obtained in the form of shiny, large plates with m.p. 99-100°, after a recrystallization from a mixture of ethyl acetate and ether (1:2).

Found %: C 58.76, 58.71; H 5.39, 5.30. $C_{11}H_{12}O_5$. Calculated %: C 58.92; H 5.39.

Cis-ortho anhydride (I) is recovered unchanged after being heated to 200° for one hour. After hydrolysis of this anhydride by boiling with water, 2-methyl-3-acetoxy-Δ^4-cyclohexene-1,2-dicarboxylic acid (III) was obtained, this acid having the m.p. 166-167° (decomp.) after repeated crystallization from water.

Found %: C 54.38, 54.45; H 5.76, 5.88. $C_{11}H_{14}O_6$. Calculated %: C 54.54; H 5.82.

An additional 0.7 g of the ortho adduct (I) and 0.5 g of the 1-methyl-$\Delta^{2,4}$-cyclohexadiene-1,2-dicarboxylic anhydride (XVII) (see below) may be isolated from the viscous, tarry product remaining, after the isolation of the crystalline products, by the way of repeated vacuum distillations and fractional crystallization. The total yield of the products of Diels-Alder condensation was about 60%. The ratio of ortho and meta adducts was about 1:1.

2-Methyl-3-hydroxy-Δ^4-cyclohexene-1,2-dicarboxylic acid (V) and its diester (VI). 1 g of cis-ortho acetoxy anhydride (I) was refluxed with 25 ml of 4% potassium hydroxide solution for one hour. The solution was acidified and evaporated to dryness under vacuum. The dry residue was extracted with boiling acetone, the solvent was distilled off under vacuum and yielded 0.65 g of cis-ortho hydroxy acid (V) with m.p. 139.5-141° (decomp.), which had m.p. 143.5-144° (decomp.) after recrystallization from ethyl acetate.

Found %: C 54.03, 54.25; H 6.07, 6.01. $C_9H_{12}O_5$. Calculated %: C 53.99; H 6.04.

The corresponding cis-ortho dimethyl ester (VI) with m.p. 61-62° (from petroleum ether) was obtained by treatment of the hydroxy acid (V) with an ethereal solution of diazomethane.

Found %: C 58.03, 57.86; H 7.06, 7.07. $C_{11}H_{16}O_5$. Calculated %: C 57.88; H 7.07.

2-Methyl-3-acetoxycyclohexane-1,2-dicarboxylic acid (VIII), its anhydride (VII) and diester (XI). 2.7 g of cis-ortho acetoxy anhydride (I) was hydrogenated in benzene solution over a palladium catalyst. One mole of hydrogen was absorbed. The solution was filtered, evaporated to dryness under vacuum, the residue was washed with ether and yielded 2.5 g of 2-methyl-3-acetoxycyclohexane-1,2-dicarboxylic anhydride (VII) with m.p. 93-94.5° (from a mixture of ethyl acetate and ether in 1:1 ratio).

Found %: C 58.49, 58.56; H 6.24, 6.30. $C_{11}H_{14}O_5$. Calculated %: C 58.39; H 6.23.

Cis-ortho acetoxy anhydride (VII) was a thermally stable substance and was recovered unchanged after having been heated for 2.5 hours at 225-230°. For hydrolysis, the acetoxy anhydride (VII) was refluxed with water and, after cooling of the solution, the cis-ortho acetoxy acid (VIII) was obtained, which had m.p. 181 to 181.5° (decomp.) after repeated recrystallization from 10% aqueous acetone.

Found %: C 54.09, 54.18; H 6.65, 6.47. $C_{11}H_{16}O_6$. Calculated %: C 54.09; H 6.63.

The corresponding diester (XI) with m.p. 66-67.5° (from petroleum ether) was obtained by treatment of the acetoxy acid (VIII) with an ethereal solution of diazomethane.

Found %: C 57.40, 57.33; H 7.45, 7.48. $C_{13}H_{20}O_6$. Calculated %: C 57.34; H 7.44.

2-Methyl-3-hydroxycyclohexane-1,2-dicarboxylic acid (IX) and its diester (X). a) 0.18 g of cis-ortho hydroxy acid (V) was hydrogenated in methanol solution over palladium catalyst, whereupon one mole of hydrogen was absorbed. The solution was filtered, evaporated to dryness under vacuum, the residue was washed with ether and yielded 0.17 g of the cis-ortho hydroxy acid (IX), which after recrystallization from ethyl acetate had m.p. 160-162° (decomp.). The substance was stable to vacuum drying at 65°.

Found %: C 53.54, 53.48; H 7.10, 7.06. $C_9H_{14}O_5$. Calculated %: C 53.45; H 6.98.

b) 0.61 g of cis-ortho diester (XI) was refluxed for 1.5 hours with 5 ml of 20% potassium hydroxide solution. The solution was acidified and allowed to stand overnight. The resulting crystals were filtered off, washed with water and, after drying in air, gave 0.3 g of cis-ortho hydroxy acid (IX) with m.p. 160-162°, which did not give a mixed melting-point depression with the above-described specimen.

The corresponding cis-ortho hydroxy diester (X) with m.p. 50.5-51.5° (from petroleum ether) was obtained by treatment of the hydroxy acid (IX) with an ethereal solution of diazomethane.

Found %: C 57.32, 57.35; H 7.95, 8.12. $C_{11}H_{18}O_5$. Calculated %: C 57.37; H 7.88.

γ-Lacto acid (XII) and its ester (XIII). a) 0.27 g of hydroxy acid (IX) was refluxed for two hours with 10 ml of 3% hydrochloric acid. The solution was evaporated to dryness in vacuum and the residue was washed with ether. 0.25 g of γ-lacto acid (XII), which had m.p. 177.5-178.5° after recrystallization from water, was obtained.

Found %: C 58.72, 58.58; H 6.48, 6.42. M 182.5 (titration with 0.01-N NaOH). $C_9H_{12}O_4$. Calculated %: C 58.69; H 6.56. M 184.19.

b) 1.45 g of acetoxy acid (VIII) was refluxed with 30 ml of 3% hydrochloric acid. After treatment similar to that described above, 1 g of γ-lacto acid (XII) with m.p. 174-176° was obtained, the product not giving a depression in a mixed melting point with the sample described above.

The corresponding ester (XIII) with m.p. 102-104° (from ether) was obtained by treatment of the γ-lacto acid (XII) with an ethereal solution of diazomethane.

Found %: C 60.23, 60.34; H 7.13, 7.08. $C_{10}H_{14}O_4$. Calculated %: C 60.59; H 7.12.

Dimethyl ester of 2-methyl-3-oxo-cyclohexane-1,2-dicarboxylic acid (XIV). A solution of 0.5 g of chromic anhydride in 12 ml of 99% acetic acid was added dropwise, with stirring at 70°, to a solution of 1.5 g of cis-ortho hydroxy diester (X) in 50 ml of glacial acetic acid. After the addition of the oxidizing agent, the reaction mixture was heated for two hours at 70°, after which 10 ml of methanol was added and the reaction mixture was set aside for overnight. The solvents were distilled off under vacuum, the residue was extracted four times with boiling benzene (in 40-ml portions), the benzene extract was washed with water and dried over magnesium sulfate. After the benzene had been distilled off, the liquid residue was distilled under vacuum. 0.92 g (61% of dimethyl ester (XIV) with b.p. 137-139° (5 mm), $n^{19}D$ 1.4735 (negative test with ferric chloride for the enol form) was isolated.

Found %: C 57.99, 57.92; H 7.21, 7.19. $C_{11}H_{16}O_5$. Calculated %: C 57.88; H 7.07.

2,4-Dinitrophenylhydrazone, obtained in the usual manner, had m.p. 160-161° (from ethanol).

Found %: C 49.84, 49.87; H 4.84, 4.93. $C_{17}H_{20}O_8N_4$. Calculated %: C 49.99; H 4.93.

Semicarbazone, prepared in the usual fashion, had m.p. 168-170° (from methanol).

Found %: C 50.65, 50.52; H 6.85, 6.76; N 14.60, 14.51. $C_{12}H_{19}O_5N_3$. Calculated %: C 50.52; H 6.71; N 14.73.

Thermal transformations of cis-meta anhydride (II). 0.8 g of cis-meta acetoxy anhydride (II) was heated for one hour to 200-205° in a stream of nitrogen. The resulting product was vacuum distilled, whereupon the

distillate crystallized immediately in the receiver. 0.38 g of 1-methyl-$\Delta^{2,4}$-cyclohexadiene-1,2-dicarboxylic anhydride (XVII) with m.p. 76-78° was obtained. Anhydride (XVII) had m.p. 83-85° after recrystallization from a mixture of ether with petroleum ether (1:1).

Found %: C 65.92, 66.05; H 5.02, 5.03. $C_9H_8O_3$. Calculated %: C 65.84; H 4.91.

Anhydride (XVII) has the characteristic absorption maximum with λ_{max} 303 mμ, lgε 3.828 (in acetonitrile) in the ultraviolet region of the spectrum. For its hydrolysis, 0.3 g of anhydride (XVII) was refluxed with water for 0.5 hour. 0.28 g of 1-methyl-$\Delta^{2,4}$-cyclohexadiene-1,2-dicarboxylic acid (XVIII) with m.p. 208-209° (from 20% aqueous acetone) was obtained.

Found %: C 59.46, 59.50; H 5.52, 5.45. $C_9H_{10}O_4$. Calculated %: C 59.33; H 5.53.

This substance has a characteristic absorption maximum with λ_{max} 285 mμ and lgε 3.793 (in ethanol) in the ultraviolet region of the spectrum.

1-Methyl-3-hydroxy-Δ^4-cyclohexene-1,2-dicarboxylic acid (XIX) and its lactonization. 1.8 g of acetoxy anhydride (II) was refluxed for one hour with 10 g of 20% aqueous potassium hydroxide solution. The solution was acidified and left overnight at room temperature. The resulting crystals were filtered off, washed with water and air-dried. 1.4 g of a mixture of crystalline products with m.p. 171-173° (decomp.) was obtained. 0.75 g of acid (XIX) with m.p. 191-194° (decomp.) was isolated after recrystallization from 8 ml of water. The melting point of the substance depends greatly on the rate and the duration of heating; however, it is unchanged after repeated recrystallizations.

Found %: C 53.96, 54.01; H 6.14, 6.03. $C_9H_{12}O_5$. Calculated %: C 53.99; H 6.04.

The mother liquor, after the isolation of the hydroxy acid (XIX), was evaporated to dryness in vacuum and 0.2 g of the same hydroxy acid was isolated from it by recrystallization of the residue from nitromethane.

For preparation of the γ-lacto acid (XX), 2.35 g of hydroxy acid (XIX) was heated for 3.5 hours with 55 ml of 12.3% sulfuric acid at 80°. The crystals which precipitated on cooling were filtered off, washed with water, and air-dried. 1.2 g of γ-lacto acid (XX) was isolated, this having the m.p. of 203-204° after recrystallization from water.

Found %: C 59.42, 59.41; H 5.67, 5.80. M 183.2 (titration with 0.01-N NaOH). $C_9H_{10}O_4$. Calculated %: C 59.33; H 5.53. M 182.4.

The corresponding γ-lacto ester (XXI), with m.p. 91-93° (recrystallization from a mixture of ethyl acetate and ether in 1:1 proportion) was prepared by treatment of the γ-lacto acid (XX) with an ethereal solution of diazomethane.

Found %: C 61.35, 61.21; H 6.11, 6.19. $C_{10}H_{12}O_4$. Calculated %: C 61.21; H 6.16.

The nitromethane mother liquor, after the isolation of hydroxy acid (XIX) (see above), was evaporated to dryness under vacuum. The residue was heated with 12.3% sulfuric acid and 0.18 g of 1-methyl-$\Delta^{2,4}$-cyclohexadienedicarboxylic acid (XVIII) with m.p. 204-205°, which did not give a depression in a mixed melting point with the specimen described above, was isolated by fractional crystallization of the resulting mixture of crystalline products from nitromethane.

1-Methyl-3-acetoxycyclohexane-1,2-dicarboxylic acid (XXVI) and its anhydride (XXII) and diester (XXVII). 3 g of cis-meta acetoxy anhydride (II) was hydrogenated in benzene solution over a palladium catalyst. One mole of hydrogen was absorbed. The solution was filtered, evaporated to dryness in vacuum, the crystalline residue was washed with ether, and 2.8 g of cis-meta acetoxy anhydride (XXII) was isolated; this had m.p. 96.5-98° (from a mixture of ethyl acetate and ether in 1:1 proportion).

Found %: C 58.50, 58.54; H 6.14, 6.26. $C_{11}H_{14}O_5$. Calculated %: C 58.39; H 6.23.

For its hydrolysis, the acetoxy anhydride (XXII) was refluxed with water until it had dissolved and, on cooling, the cis-meta acetoxy acid (XXVI) with m.p. 190° (decomp.) crystallized out quantitatively.

Found %: C 53.86, 53.86; H 6.59, 6.39. $C_{11}H_{16}O_6$. Calculated %: C 54.09; H 6.63.

The corresponding diester (XXVII) with m.p. 71-73° (from petroleum ether) was prepared by treatment of the acetoxy acid (XXVI) with an ethereal solution of diazomethane.

Found %: C 57.40, 57.33; H 7.45, 7.48. $C_{15}H_{20}O_6$. Calculated %: C 57.34; H 7.44.

Thermal transformation of acetoxy anhydride (XXII). 5.5 g of cis-meta acetoxy anhydride (XXII) was heated at 225-230° for 2.5 hours in a stream of nitrogen, whereupon a distillation of acetic acid was observed. The liquid residue was distilled under vacuum of 3.5 mm and two fractions were collected: 1st – b.p. 119-125°, 2 g; 2nd – b.p. 125-128°, 1.8 g. By freezing-out at 0°, 0.65 g of a crystalline product was obtained from the first fraction and 1.63 g from the second fraction, this product having m.p. 61-63°, after being washed with petroleum ether. Both portions gave no mixed melting-point depression with each other. 1-Methyl-Δ^2-cyclohexene-1,2-dicarboxylic anhydride (XXIII), with m.p. 69-70°, was obtained after recrystallization from a mixture of ether with petroleum ether (1:2).

Found %: C 64.87, 64.94; H 5.86, 6.08. $C_9H_{10}O_3$. Calculated %: C 65.04; H 6.07.

An additional 0.20 g of anhydride (XXIII) and 0.55 g of a liquid product, with b.p. 119-127° (3.5 mm), was isolated from the liquid pyrolysis product by redistillation under vacuum and a freezing-out at 0°; the liquid product, on hydrogenation in benzene solution over a palladium catalyst, gave 0.32 g of cis-1-methylcyclohexane-1,2-dicarboxylic anhydride with m.p. 68-70°, which did not give a mixed melting-point depression with an authentic specimen [5].

For the hydrolysis, anhydride (XXIII) was refluxed for 30 minutes with 25% aqueous acetone and 1-methyl-Δ^2-cyclohexene-1,2-dicarboxylic acid (XXIV), with m.p. 236° (decomp.), was obtained.

Found %: C 58.90, 59.02; H 6.57, 6.60. $C_9H_{12}O_4$. Calculated %: C 58.68; H 6.56.

In order to prove the location of the double bond, 1 g of acid (XXIV) was ozonized in a solution of 80 ml of 92% acetic acid (one hour; ozone concentration 0.4 g/hour). 10 ml of 70% peracetic acid was added to the solution and the mixture was heated for 24 hours at 45-50°. The solution was evaporated to a volume of 10 ml, 2 ml of 70% peracetic acid was added, and the whole was heated for six hours longer at 50°. The volatile products were distilled off under vacuum, the residue was heated for one hour at 130-140° and, after this, it was distilled under vacuum (at 6 mm). 0.58 g of α-methyladipic acid was isolated, from which the diamide with m.p. 185-186° was obtained by the usual method. According to [6], the diamide has m.p. 186.5°.

γ-Lacto acid (XXVIII) and its ester (XXIX). 0.8 g of acetoxy acid (XXVI) was refluxed for two hours with 3% hydrochloric acid. The solution was evaporated to dryness in vacuum and the residue was washed with ether, yielding 0.52 g of acid (XXVIII) with m.p. 182-183° (from water).

Found %: C 58.58, 58.52; H 6.58, 6.54. $C_9H_{12}O_4$. Calculated %: C 58.63; H 6.56.

The corresponding γ-lacto ester (XXIX) with m.p. 86-87° (from petroleum ether) was obtained quantitatively on treatment of the γ-lacto acid (XXVIII) with an ethereal solution of diazomethane.

Found %: C 60.77, 60.57; H 7.15, 7.18. $C_{10}H_{14}O_4$. Calculated %: C 60.59; H 7.12.

The same γ-lacto ester (XXIX) was obtained quantitatively by hydrogenation of the unsaturated γ-lacto ester (XXI) in methanol solution over a palladium catalyst.

Alkaline hydrolysis of acetoxy ester (XXVII). 3 g of acetoxy diester (XXVII) was refluxed with 16 ml of 20% aqueous potassium hydroxide solution for two hours, after which the solution was filtered, acidified with concentrated hydrochloric acid and set aside for twelve hours at room temperature. The precipitated crystals were filtered off, yielding 1.42 g of a mixture of crystalline products with m.p. 170-188°. 0.7 g of a substance with m.p. 210-214° was isolated after recrystallization from 50% aqueous acetone. Repeated recrystallization of this from 50% aqueous acetone permitted us to obtain 0.4 g of 1-methyl-Δ^2-cyclohexene-1,2-dicarboxylic acid (XXIV) with m.p. 231-233°, which failed to give a depression in a mixed melting point with the specimen described above. 0.37 g of γ-lacto acid (XVIII) with m.p. 178-180°, which did not give a depression in a mixed melting point with the above-described specimen, was obtained from the mother liquor from the first crystallization, by evaporation and recrystallization of the residue from water. An additional 0.5 g of the γ-lacto acid (XXVIII) with m.p. 180-183° was isolated after the main acidic mother liquor had stood for three days.

1-Methyl-3-hydroxycyclohexane-1,2-dicarboxylic acid (XXX) and its lactonization. 0.5 g of the hydroxy acid (XIX) was hydrogenated in a methanol solution over a palladium catalyst. One mole of hydrogen was absorbed. The solution was filtered and evaporated to dryness in vacuum. 0.5 g of 1-methyl-3-hydroxycyclohexane-1,2-dicarboxylic acid (XXX) was obtained, which did not have a sharp melting point, owing to the ease of

its lactonization after even a slight heating; hence, the hydroxy acid (XXX) could not be analyzed. Its structure was proved by the fact that, on being heated for one hour at 150°, or after a two-hour boiling with 3% hydrochloric acid, it was quantitatively converted into the above-described γ-lacto acid (XXVIII) with m.p. 180-183°.

SUMMARY

1. It was shown that a mixture of both possible structural isomers (I) and (II) is formed in approximately 1:1 proportion during the condensation of 1-acetoxybutadiene with citraconic anhydride.

2. The structure and the configuration of the isomeric ortho and meta adducts was proved by the study of the reactions of cleavage and lactonization.

3. The conformations were examined for all the above-described derivatives of 1- and 2-methyl-3-hydroxycyclohexane-1,2-dicarboxylic acids and the peculiarities of their chemical transformations were explained.

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••See C.B. translation.

A STUDY IN THE FIELD OF STEREOCHEMISTRY OF CYCLIC COMPOUNDS

XXXI. STEREOCHEMISTRY OF OXIDATION OF ANTI-CIS-Δ^4-OCTAHYDRONAPHTHALENE-1,2-DICARBOXYLIC ACID

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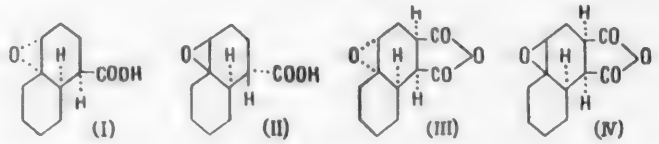
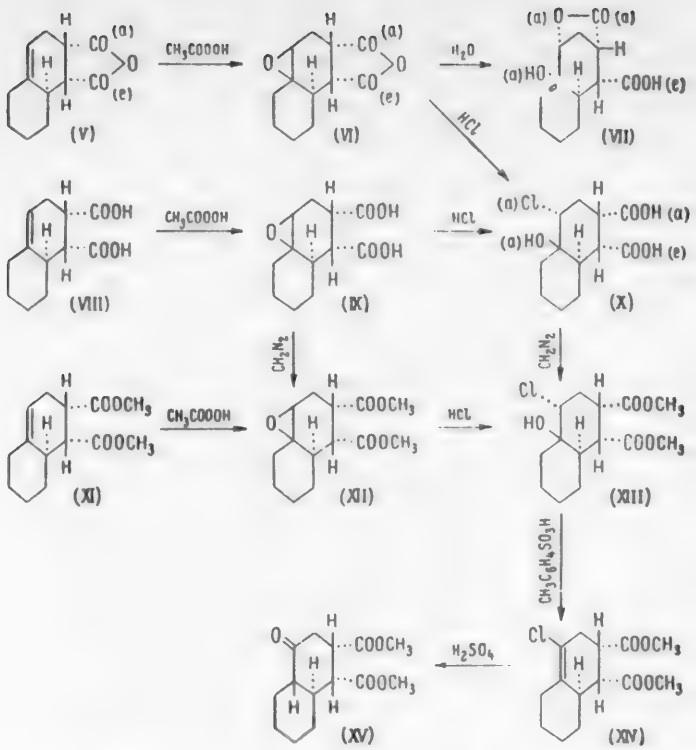
It was shown by us in the previous papers [1, 2] that the oxidation of isomeric syn- and anti-Δ^4-octahydronaphthalene-1-carboxylic acids with peracetic acid proceeds with steric specificity from the side opposite to the carboxyl groups and leads solely to α-oxides (I) and (II). In contrast to this, syn-cis-Δ^4-octahydronaphthalene-1,2-dicarboxylic anhydride is oxidized without steric specificity [3] and yields a mixture of isomeric oxides (III) and (IV), the configuration of which could be proved by a series of stereospecific transformations.



In the present paper we consider the experimental data on the stereochemistry of oxidation of the isomeric anti-cis-Δ^4-octahydronaphthalene-1,2-dicarboxylic acid and its derivatives with peracetic acid, as well as the data on the reaction of cis-hydroxylation with osmic anhydride as applied to both isomeric syn-cis and anti-cis anhydrides. It turned out that the oxidation of anti-cis-Δ^4-octahydronaphthalene-1,2-dicarboxylic anhydride (V) with peracetic acid proceeds sterically specifically, in contrast to the reaction of the isomeric syn-cis anhydride, and leads, in yields of above 85%, to the individual α-oxide (VI), the configuration of which corresponds to the disposition of the oxide ring at the side opposite to the carboxyl groups [4]. The α-oxide (VI), on being boiled with water, is readily transformed into the hydroxy-γ-lacto acid (VII), which undergoes a deepseated oxidative cleavage during oxidation with chromic anhydride in acetic acid and does not yield the corresponding keto-γ-lacto acid. This fact indicates that a tertiary carboxyl group is present in the hydroxy-γ-lacto acid (VII), the origin of this group being possible only as a result of a trans-diaxial opening of the oxide ring at the site of the C—O bond at C_4 position, with the subsequent lactonization at the axial carboxyl at C_2 position.

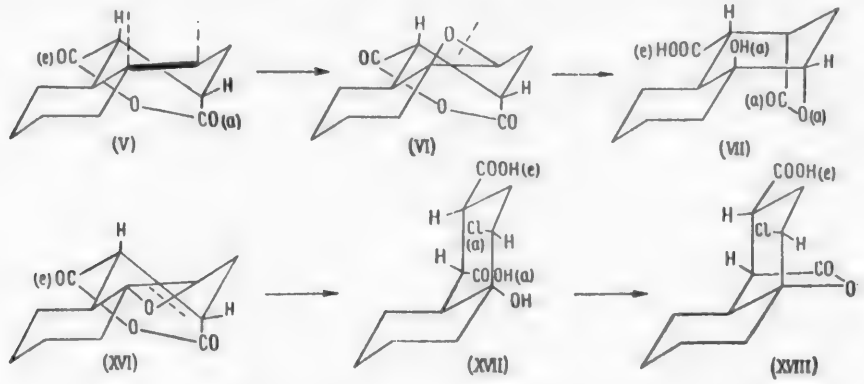
The oxidation of anti-cis-Δ^4-octahydronaphthalene-1,2-dicarboxylic acid (VIII) proceeds similarly and leads to a mixture of the corresponding α-oxide (IX) and hydroxy-γ-lacto acid (VII).

Oxides (VI) and (IX) readily yield the same trans-chlorohydrin (X) under the influence of hydrogen chloride and the configuration of this product must correspond to the trans-diaxial opening of the oxide ring. In order to prove the structure of this chlorohydrin, we studied some transformations of the diester (XIII) which corresponds to it, this ester having been also prepared from the diester α-oxide (XII), isolated on oxidation of anti-cis diester (XI). It turned out that the diester of trans-chlorohydrin (XIII) contains a tertiary hydroxyl group at C_{10} position and readily yields the unsaturated chloro diester (XIV) during a dehydration with p-toluenesulfonic acid; hydrolysis of the latter led to the previously described trans-anti-cis-4-oxo diester (XV) [5]. These transformations singularly



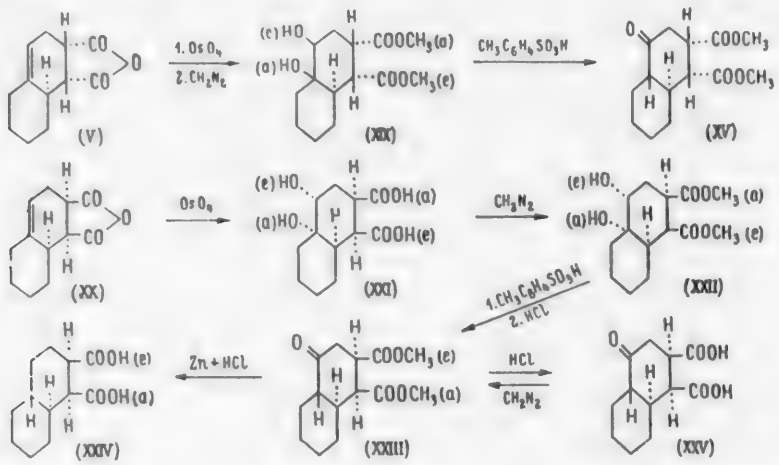
prove the structure of the trans-chlorohydrin (X) and its diester (XIII), the formation of which, as well as the formation of the hydroxy-γ-lacto acid (VII), occurs as a result of rupture of the oxide bond at C_4 position.

This nature of the oxide ring opening, with facile lactonization into the hydroxy-γ-lacto acid (VII), simultaneously proves its α-configuration as well (disposition from the side opposite to the carboxyl groups). This is visually confirmed by the examination of molecular models from which it is evident that if the oxides had the opposite β-configuration (XVI), the opening of the oxide ring in them from the side of C_4, under the action of hydrogen chloride, would have led to the trans-chlorohydrin of cis-decahydronaphthalene series (XVII), capable of a facile lactonization into the chloro-γ-lacto acid (XVIII), which was not observed in reality.



The cis-hydroxylation of the anti-cis anhydride (V) with osmic anhydride also occurs from the side opposite to the carboxyl groups. The diester of cis-glycol (XIX), isolated from this reaction, contains an axial hydroxyl group at C_{10}, as a result of which it is readily dehydrated on being heated with p-toluenesulfonic acid and yields the above-described trans-anti-cis-4-oxo diester (XV). Cis-hydroxylation of the isomeric syn-cis anhydride (XX) also occurs similarly. In this case, it is possible to isolate the corresponding cis-glycol of cis-decahydronaphthalene series (XXI), whose diester (XXII) yields trans-syn-cis-4-oxo diester (XXIII), with a trans-joining of the rings [6], after the dehydration with a subsequent treatment with hydrochloric acid. The configura-

tion of the latter substance could be proved by the fact that by a Clemmensen reduction it was transformed into the previously described trans-syn-cis acid (XXIV) [7], while on hydrolysis with hydrochloric acid, it gave the corresponding trans-syn-cis-4-oxo acid (XXV) transformed, after treatment with diazomethane, into the original trans-syn-cis-4-oxo diester (XXIII).



As is evident from these transformations, the cis-hydroxylation reaction of isomeric syn-cis and anti-cis-Δ^4-octahydronaphthalene-1,2-dicarboxylic acids with osmic anhydride may be a convenient method for the synthesis of stereoisomeric 4-oxodecahydronaphthalene-1,2-dicarboxylic acids, including those which could not be obtained by the Diels-Alder condensations employing 1-α-acetoxyvinyl-Δ^1-cyclohexene [5].

EXPERIMENTAL

Oxidation of anti-cis-Δ^4-octahydronaphthalene-1,2-dicarboxylic anhydride (V). 2.8 ml of 80% peracetic acid was added to the solution of 4.8 g of anti-cis-anhydride (V) [8] in 50 ml of dry chloroform and the mixture was set aside at the same temperature (0°) overnight. The chloroform and the excess peracetic acid were distilled off under vacuum and the crystalline residue was washed on the filter with a mixture of ether and petroleum ether (4:1). 4.3 g (85.5%) of α-oxide (VI) with m.p. 154-156° was obtained, and this had m.p. 156-157° after recrystallization from benzene.

Found %: C 64.62, 64.71; H 6.41, 6.36. $C_{12}H_{14}O_4$. Calculated %: C 64.75; H 6.34.

Transformations of the α-oxide (VI). a) A solution of 1 g of the α-oxide (VI) in a mixture of 20 ml of dioxane and 4 ml of water was refluxed for 20 hours, after which the solvents were distilled off in vacuum and the residue was treated with ether. 0.65 g of hydroxy-γ-lacto acid (VII) with m.p. 203-205° was obtained, which melted at 207-208° after recrystallization from a mixture of acetone and ether (1:1).

Found %: C 59.87, 59.81; H 6.67, 6.64. $C_{12}H_{16}O_5$. Calculated %: C 60.0; H 6.71.

The corresponding methyl ester, which had m.p. 127-128° after recrystallization from ether, was prepared by treatment of the hydroxy-γ-lacto acid (VII) with an ethereal solution of diazomethane.

Found %: C 61.28, 61.13; H 7.16, 7.17. $C_{13}H_{18}O_5$. Calculated %: C 61.40; H 7.13.

b) 2 ml of concentrated hydrochloric acid was added to the ethereal solution of 1 g of α-oxide (VI) and the mixture was left overnight at room temperature. 0.75 g of trans-chlorohydrin (X) was isolated, this having the m.p. 203-204° after a recrystallization from dioxane.

Found %: C 52.21, 52.27; H 6.05, 6.13; Cl 12.75, 12.71. $C_{12}H_{17}O_5Cl$. Calculated %: C 52.06; H 6.19; Cl 12.81.

Oxidation of anti-cis-Δ^4-octahydronaphthalene-1,2-dicarboxylic acid (VIII). 2.8 ml of 80% peracetic acid was gradually added at 0° to a solution of 5 g of anti-cis acid (VIII) [8] in 50 ml of dry chloroform and the mixture was left overnight at room temperature. The solvent was removed under vacuum and the semi-solid residue was treated with 5 ml of ether. 1.4 g of α-oxide (IX) with m.p. 167-168°, unchanged after recrystallization from acetone, was isolated.

Found %: C 59.81, 59.88; H 6.88, 6.75. $C_{12}H_{16}O_5$. Calculated %: C 60.0; H 6.71.

0.55 g of a crystalline product with m.p. 185-192° separated from the ethereal mother liquor after standing for several days and recrystallization of this from a mixture of acetone and ether (1:1) gave 0.4 g of the above-described hydroxy-γ-lacto acid (VII) with m.p. 207-208°. The residue, after the isolation of hydroxy-γ-lacto acid (VII), was treated with an ethereal solution of hydrogen chloride, as a result of which 1.5 g of trans-chlorohydrin (X), with m.p. 202-204°, which did not give a mixed-melting-point depression with the above-described specimen, was isolated.

Oxidation of the diester of anti-cis-Δ^4-octahydronaphthalene-1,2-dicarboxylic acid (XI). 3 ml of 80% peracetic acid was added with cooling to a solution of 6.2 g of the anti-cis diester (XI) [8] in chloroform and the solvent was distilled off after the mixture had stood overnight. The resulting crystalline oxidation product was washed on the filter with a mixture of ether and petroleum ether (1:2) and 5.2 g of the diester of α-oxide (XII) with m.p. 111-112°, was isolated after two recrystallizations from the same solvent mixture.

Found %: C 62.74, 62.60; H 7.57, 7.53. $C_{14}H_{20}O_5$. Calculated %: C 62.67; H 7.51.

The same diester of α-oxide (XII) was obtained in a quantitative yield by treatment of the α-oxide (IX) with an ethereal solution of diazomethane.

Dimethyl ester of trans-chlorohydrin (XIII) and its transformations. 1.4 g of the diester of α-oxide (XII) was dissolved in 30 ml of ether saturated with dry hydrogen chloride and the solution was set aside at room temperature. The separated reaction product was filtered off after 20 hours and yielded 1.1 g of dimethyl ester of the trans-chlorohydrin (XIII) with m.p. 161-162° after recrystallization from a mixture of acetone and ether.

Found %: C 55.12, 55.22; H 7.03, 6.85; Cl 11.68, 11.61. $C_{14}H_{21}O_5Cl$. Calculated %: C 55.12; H 6.93; Cl 11.63.

The same diester (XIII) is obtained quantitatively by treatment of the trans-chlorohydrin with an ethereal solution of diazomethane.

1 g of the diester of trans-chlorohydrin (XIII) was heated in the presence of a small amount of p-toluenesulfonic acid under vacuum at 165-170° for the purpose of dehydration. The reaction product was dissolved in ether, the extract was washed with water, dried and freed of ether by distillation. The resulting oil crystallized partially and, after having been washed with a mixture of ether and petroleum ether (1:1), this gave 0.35 g of the unsaturated chloro diester (XIV) with m.p. 62-64°, which had m.p. 64.5-65° after recrystallization from ether.

Found %: C 53.47, 53.38; H 8.05, 7.96; Cl 13.45, 13.41. $C_{14}H_{19}O_4Cl$. Calculated %: C 53.35; H 8.0; Cl 13.39.

For hydrolysis, 0.2 g of the unsaturated chloro diester (XIV) was dissolved at 0° in 0.5 ml of concentrated sulfuric acid and, after standing for three hours at this temperature, was poured into 5 ml of water. The mixture was heated at 50° for 30 minutes longer, after which it was thoroughly extracted with ether, and the ethereal solution was treated with diazomethane; ether was distilled from the mixture and the residue was treated with an alcoholic solution of 2,4-dinitrophenylhydrazine. 0.1 g of 2,4-dinitrophenylhydrazone of trans-anti-cis-4-oxo diester (XV) with m.p. 209-210° was obtained; this gave no depression in a mixed melting point with a previously prepared specimen [5].

Diester of cis-glycol (XIX) and its transformations. 2 g of osmic anhydride was added to an ethereal solution of 1.5 g of anti-cis anhydride (V) and the mixture was set aside for five days at room temperature. Ether was then distilled from it and the residue was dissolved in 100 ml of ethyl alcohol, treated with 14.4 g of sodium sulfite in 70 ml of water, and the whole was refluxed with stirring for four hours. The resulting precipitate was filtered off, washed with 50% alcohol, the combined mother liquors were concentrated to the volume of 10 ml, and were acidified with hydrochloric acid to Congo red. The resulting crystalline glycol was filtered off, washed with cold water, dried in air and treated with an ethereal solution of diazomethane. The ether was distilled off and there was formed 1.2 g of the crystalline diester of cis-glycol (XIX) with m.p. 102-104°, which melted at 106-107° after recrystallization from a mixture of ether and petroleum ether (2:1).

Found %: C 58.89, 58.80; H 7.79, 7.79. $C_{14}H_{22}O_6$. Calculated %: C 58.73; H 7.74.

The trans-anti-cis-4-oxo diester (XV), with m.p. 99-100°, which gave no mixed-melting-point depression

with a specimen prepared earlier [5], was isolated in good yield after the dehydration of the above substance with p-toluenesulfonic acid (2,4-dinitrophenylhydrazone has m.p. 210-212°).

Diester of cis-glycol (XXII) and its transformations. 3.1 g of the diester of cis-glycol (XXII), which had m.p. 122-123° after recrystallization from a mixture of ether and methanol (5:1), was isolated by the above-described method from 3 g of syn-cis anhydride (XX) [8].

Found %: C 58.76, 58.60; H 7.78, 7.71. $C_{14}H_{22}O_6$. Calculated %: C 58.73; H 7.74.

Trans-syn-cis-4-oxo diester (XXIII) with m.p. 92-94°, which had been described previously [6], and which gave in good yield the known trans-syn-cis-4-oxodecahydronaphthalene-1,2-dicarboxylic acid (XXV) with m.p. 143-144° [6] on hydrolysis with hydrochloric acid, was obtained by heating the diester of cis-glycol (XXII) with p-toluenesulfonic acid with a subsequent treatment of the dehydration product with hydrochloric acid.

SUMMARY

1. The reaction of oxidation with peracetic acid of anti-cis-Δ^4-octahydronaphthalene-1,2-dicarboxylic acid (VIII), its anhydride (V) and diester (XI), which leads to the corresponding α-oxides (IX), (VI) and (XII), whose configuration was proved by a series of stereospecific transformations, was studied.

2. The cis-hydroxylation of syn-cis- and anti-cis anhydrides (XX) and (V) was studied and the resulting isomeric cis-glycols (XIX) and (XXII) were utilized for stereospecific synthesis of isomeric 4-oxodecahydronaphthalene-1,2-dicarboxylic acids.

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α-KETO OXIDES

IX. OXIDES OF ALKYLIDENEACETONES AND SOME OTHER α,β-UNSATURATED KETONES

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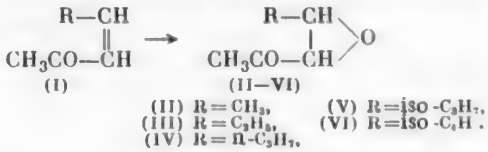
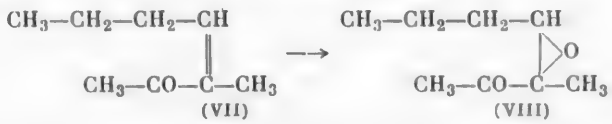
The ability of divinyl ketones, vinyl propenyl ketones and the corresponding unsaturated β-methoxy ketones to oxidize under the influence of alkaline hydrogen peroxide to the corresponding α-keto oxides and α-keto dioxides in high yields was described in the previous papers of this series [1, 2, 3]. The resulting keto oxides readily react with substances containing active hydrogen and are therefore of interest for synthetic purposes.

We decided, for the further study of α-keto oxides, to accomplish the oxidation reaction with alkaline hydrogen peroxide [4] for other α,β-unsaturated ketones of the aliphatic series, which belong mainly to the series of alkylideneacetones. We were urged in this direction also by the fact that only the isopropylideneacetone oxide (oxide of mesityl oxide) has been described up to the present [4, 5] of the various alkylideneacetone oxides that are possible. The remaining oxides in this series of ketones are still unknown. The present communication is devoted to the study of oxidation with alkaline hydrogen peroxide of: ethylideneacetone (2-penten-4-one), propylideneacetone (3-hexen-2-one), trans-n-butylideneacetone (3-hepten-2-one), trans-isobutylideneacetone (5-methyl-3-hexen-2-one), isoamylideneacetone (6-methyl-3-hepten-2-one), as well as 3-methyl-3-hepten-2-one, 1-methoxy-5-methyl-4-octen-3-one and 5-methyl-1,4-octadien-3-one.

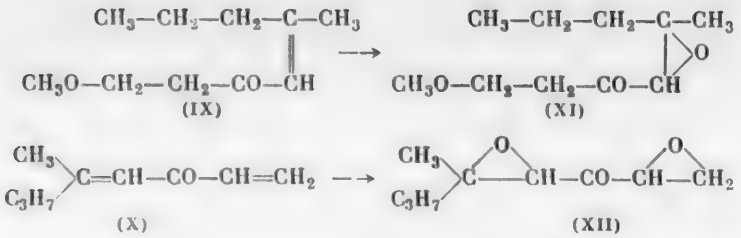
It was established thereby that the corresponding α-keto oxides (II-VI) are formed by the action with alkaline hydrogen peroxide on the alkylideneacetones (I) in methanolic solution with cooling.



Similarly, 3-methyl-3,4-epoxy-2-heptanone (VIII) is formed by the action of alkaline hydrogen peroxide on 3-methyl-3-hepten-2-one (VII) in methanolic solution,



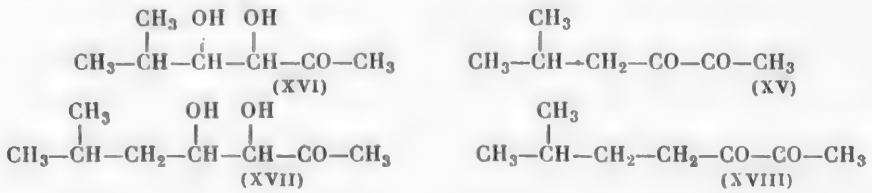
while 1-methoxy-5-methyl-4-octen-3-one (IX) and 5-methyl-1,4-octadien-3-one (X) yield, respectively, 1-methoxy-5-methyl-4,5-epoxy-3-hexanone (XI) and 5-methyl-1,2,3,4-diepoxy-3-octanone (XII).



It is of interest to note that the presence of alkyl groups at the double bond in the three latter ketones (VII, IX, X) greatly hinders the oxidation of the latter with alkaline hydrogen peroxide, a fact to which attention had been called previously [2, 8] and which had been noted by other workers [6]; this is evidently explained by the electron-repelling action of the alkyl radicals and the nucleophilic nature of the peroxide ion HO_2^- which attacks the double bond. At the same time, the alkyl groups located at the double bond exert, as it is known, a positive effect in reactions of oxidation of unsaturated compounds by hydroperoxides of acids [9, 10]. The oxidation of these ketones, in contrast to that of the alkylideneacetones, was run with a considerable excess of alkaline hydrogen peroxide at room temperature. Alkylideneacetone oxides turned out to be stable in respect to the action of water. Thus, ethylideneacetone oxide (3,4-epoxy-2-pentanone) (II) is hydrolyzed to 3,4-dihydroxy-2-pentanone only after an extended heating of its aqueous solution on a steam bath and the yield of the keto glycol is low. The reaction of hydrolysis of α-keto oxides is accelerated considerably in the presence of small amounts of sulfuric acid; however, the isomerization of the α-keto axides into α-diketones occurs in this case along with the formation of keto glycols. The formation of these substances becomes predominant in a number of cases, which opens the way for a possible preparation of α-diketones by isomerization of α-keto oxides. Thus, for example, propylideneacetone oxide (3,4-epoxy-2-hexanone) (III) isomerizes into the known acetylbutyryl (2,3-hexanedione) after a brief heating at reflux with 1% sulfuric acid solution [7, 10]. Trans-n-butylideneacetone oxide (3,4-epoxy-2-heptanone) (IV) isomerizes into 2,3-heptanedione (XIII) on being refluxed with 0.5% sulfuric acid solution and simultaneously yields the keto glycol (3,4-dihydroxy-2-heptanone) (XIV) in the proportion of 2:1, by hydrolysis.

The structure of heptanedione (XIII) was proved by its cleavage into n-valeric and acetic acids under the influence of excess alkaline hydrogen peroxide [4].

During the hydrolysis of oxides of trans-isobutylideneacetone (2-methyl-3,4-epoxy-5-hexanone) (V) and isoamylideneacetone (2-methyl-4,5-epoxy-6-heptanone) (VI) under the same conditions, the known acetylisovaleryl (2-methyl-4,5-hexanedione) (XV) [7, 8, 12], 2-methyl-3,4-dihydroxy-5-hexanone (XVI), the keto glycol (2-methyl-4,5-dihydroxy-6-heptanone) (XVII) and acetylisocaproyl (2-methyl-5,6-heptanedione) (XVIII) [7, 13] are formed, respectively, under the same conditions.



It is of interest to note that 3-methyl-3,4-epoxy-2-heptanone (VIII) isomerizes under the influence of 2% sulfuric acid into 4-methyl-2,3-heptanedione (XIX) with the simultaneous migration of the methyl group from α- to β-carbon atom position, similarly to the one observed by us earlier [14]. During the action of excess alkaline hydrogen peroxide in the α-diketone (XIX) [4], the latter is cleaved at 2,3-position for formation of the corresponding acids, which confirm its structure.

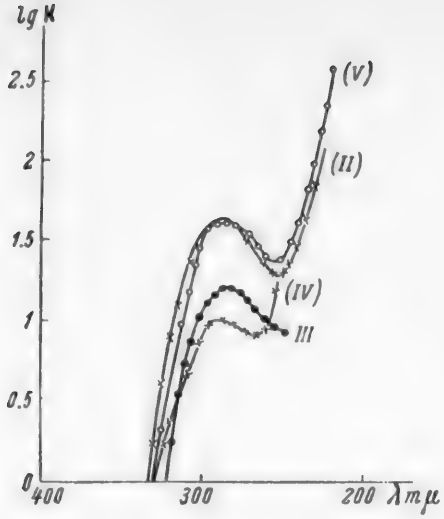


Fig. 1. Ultraviolet absorption spectra (in anhydrous alcohol): (II) – ethylideneacetone oxide; (III) – propylideneacetone oxide; (IV) – trans-n-butylideneacetone oxide; (V) – isobutylideneacetone oxide. Alkylideneacetone oxides have similar absorption curves in the ultraviolet with an intense absorption band at 285-290 mμ [15].

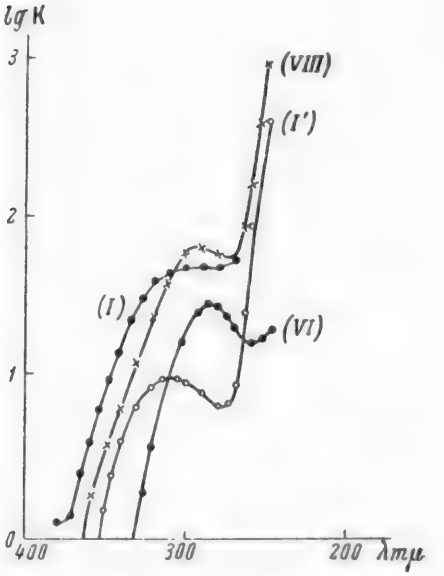


Fig. 2. Ultraviolet absorption spectra (in anhydrous alcohol): (I) (R = n-C_3H_7) – trans-n-butylideneacetone [16]; (I') (R = iso-C_4H_9) isoamylideneacetone [16]; (VI) – isoamylideneacetone oxide; (VIII) – 3-methyl-3-hepten-2-one oxide.

$$(VIII) \rightarrow CH_3CH_2\text{—}CH_2\text{—}\underset{(XIX)}{\underset{|}{\overset{CH_3}{CH}}}\text{—}CO\text{—}CO\text{—}CH_3 \rightarrow$$

$$\rightarrow CH_3\text{—}CH_2\text{—}CH_2\text{—}\underset{|}{\overset{CH_3}{CH}}\text{—}COOH + CH_3COOH$$

We also examined the ultraviolet absorption spectra of the alkylideneacetone oxides prepared by us (II-VI) and of 3-methyl-3-hexen-2-one oxide (VIII) in the wavelength region from 200 to 400 mμ. The measurements were made with the photoelectric quartz spectrophotometer SF-4. The absorption spectra of these compounds are shown in Figs. 1 and 2.

EXPERIMENTAL

1. Oxidation of Ethylideneacetone (I, R = CH_3)

61 g of ethylideneacetone (b.p. 121-122°, $n^{17}D$ 1.4390), prepared by condensation of acetaldehyde with acetone in an alkaline medium [17], was diluted with 320 ml of methanol and to the solution, cooled to −8 to −10°, placed in a three-necked flask with a thermometer, a mechanical stirrer and two dropping funnels, there was added simultaneously and with good stirring, 150 ml of 18% hydrogen-peroxide solution and 28 ml of 4-N aqueous sodium-hydroxide solution. The addition of the oxidizing agent was run at such a rate that the temperature of the reaction mixture did not rise over −5 to −6°, which required about two hours with good cooling of the reaction flask with ice-salt mixture. After the introduction of the oxidizing agent, the reaction mixture was stirred with cooling for 2.5-3 hours longer. Then the sodium hydroxide was neutralized with 10% sulfuric acid; the excess hydrogen peroxide that was used (2.7 g) was decomposed by the addition of manganese dioxide to the reaction mixture. The solution was diluted with an equal volume of water, saturated with powdered sodium chloride, the product was extracted three times with ether, the extract dried over magnesium sulfate and distilled in vacuum, after the removal of ether by distillation. 40 g (56.5%) of 3,4-epoxy-2-pentanone (II) was isolated in the form of a colorless, mobile liquid with a weak characteristic odor.*

B.p. 44-45° (11 mm), 48° (14 mm), d^{20}_4 0.9818, $n^{20}D$ 1.4162, MR_D 25.57; calc. 25.45. λ_{max} 285 mμ (clear).

Found %: C 60.32, 60.14; H 8.22, 8.14. M 102, 101.8. $C_5H_8O_2$. Calculated %: C 60.00; H 8.00. M 100.

The 2,4-dinitrophenylhydrazone precipitated only after a prolonged standing of the alcoholic solution of the oxide with a sulfuric-acid solution of 2,4-dinitrophenylhydrazine at room temperature or after a mild heating; it formed characteristic, small, orange colored crystals with m.p. 241-242° (from a mixture of alcohol and ethyl acetate).

*Ethylideneacetone, prepared by the reaction of paraldehyde with acetone in the presence of hydrogen chloride [18], oxidizes less smoothly.

Found %: N 20.59, 20.35. $C_{11}H_{12}O_5N_4$. Calculated %: N 20.00.

Ethylideneacetone oxide is readily soluble in water and the usual organic solvents. It displays an acid reaction after prolonged storage in air.

Hydrolysis of ethylideneacetone oxide (II). 12.5 g of the keto oxide (II) dissolved in 60 ml of distilled water, was heated under a reflux condenser on a steam bath for 25 hours. The cooled solution was saturated with potassium carbonate, the product was repeatedly extracted with ether, the ethereal extracts were combined and dried with magnesium sulfate and the reaction products were vacuum distilled, after the distillation of ether. 2.7 g of 3,4-dihydroxy-2-pentanone, in the form of a viscous, colorless liquid which was odorless, was obtained.

B.p. 108-109° (14 mm), d^{20}_4 1.1085, $n^{20}D$ 1.4542, MR_D 28.74; calc. 28.55.

Found %: C 50.62, 50.77; H 8.49, 8.63; OH 29.20, 29.07. $C_5H_{10}O_3$. Calculated %: C 50.85; H 8.47; OH 28.81.

The 2,4-dinitrophenylhydrazone – small, needle-shaped crystals with orange color and m.p. 245-247° (from a mixture of ethyl alcohol and ethyl acetate).

Found %: N 18.81, 18.89. $C_{11}H_{14}O_6N_4$. Calculated %: N 18.79.

2. Oxidation of Propylideneacetone (I, R=C_2H_5)

18.4 g of propylideneacetone (b.p. 136-138°, $n^{17}D$ 1.4445), prepared by the condensation of propionaldehyde with acetone in an alkaline medium [19], was oxidized in 100 ml of methanol as described above. 12.2 g (57.2%) of 3,4-epoxy-2-hexanone (III) was obtained in the form of a colorless liquid with a characteristic, rather pleasant odor.

B. p. 60-61° (14 mm), 56-56.5° (12 mm), d^{20}_4 0.9723, $n^{20}D$ 1.4252, MR_D 29.97; calc. 30.06. λ_{max} 285 mμ (in alcohol).

Found %: C 62.72, 62.83; H 8.45, 9.19. M 117, 116. $C_6H_{10}O_2$. Calculated %: C 63.16; H 8.78. M 114.0.

The 2,4-dinitrophenylhydrazone – orange crystals with an m.p. 223-224° (from a mixture of ethanol and ethyl acetate).

Found %: N 19.55. $C_{12}H_{14}O_5N_4$. Calculated %: N 19.05.

The keto oxide is soluble in water (1:6 at 17°) and in the usual organic solvents.

Isomerization of propylideneacetone oxide (III). A solution of 4.2 g of the keto oxide in 25 ml of 1% sulfuric acid was refluxed. Soon after the beginning of boiling, drops of yellow-green oil begin to run down the condenser along with water. After 3.5 hours, the cooled solution was saturated with powdered salt, the product was extracted with ether, dried with magnesium sulfate and distilled. About 2 g of acetylbutyryl (2,3-hexanedione) was obtained in the form of a yellow-green oil with a penetrating, sharp odor, with b.p. 128-129°, d^{18}_4 0.9353 [11].

Its dioxime was prepared by careful and brief heating of an alcoholic solution of the diketone with hydroxylamine hydrochloride. Colorless plates with m.p. 168-169° (from alcohol) [7, 20].

Found %: N 19.83. $C_6H_{12}O_2N_2$. Calculated %: N 19.44.

The diketone displays an acid reaction after prolonged storage.

3. Oxidation of Trans-n-Butylideneacetone (I, R=C_3H_7)

The trans-n-butylideneacetone used for the oxidation was prepared by condensation of butyraldehyde with acetone under mild conditions in the presence of alkali [21]. Here, 4-heptanol-2-one was formed as the main reaction product and the trans-butylideneacetone formed only in a small amount.

For the preparation of butylideneacetone, the resulting keto glycol was distilled under vacuum (15 mm), in the presence of a trace of concentrated sulfuric acid. Pure trans-butylideneacetone was formed thereby in 81% yield. The previous methods of the dehydration of keto glycol with anhydrous oxalic acid and crystalline iodine failed to give a satisfactory result.

To a solution of 116 g of trans-butylideneacetone (b.p. 62° at 15 mm, $n^{20}D$ 1.4430, d^{20}_4 0.8444) in 550 ml of methanol, placed in a three-necked flask, there was added, with energetic stirring at −8 to −10° over 1.5 hours, 205 ml of 18% hydrogen-peroxide solution and 18 ml of 4-N aqueous sodium-hydroxide solution. 94.5 g (71.3%) of 3,4-epoxy-2-heptanone (IV) was isolated in the form of a colorless, mobile liquid with a characteristic, pleasant odor.

B.p. 54.5-55° (5 mm), d^{20}_4 0.9518, $n^{20}D$ 1.4292, MR_D 34.64; calc. 34.68. λ_{max} 285 mμ (in alcohol).

Found %: C 65.30, 65.32; H 9.69, 9.12. M 127.5, 127.4. $C_7H_{12}O_2$. Calculated %: C 65.62; H 9.38; M 128.

The 2,4-dinitrophenylhydrazone – characteristic, crumbly, silky crystals with yellow-orange color; m.p. 141-142° (from alcohol).

Found %: N 18.28. $C_{13}H_{16}O_5N_4$. Calculated %: N 18.18.

The keto oxide is poorly soluble in water, readily soluble in the usual organic solvents. It is stable in storage.

Hydrolysis and isomerization of trans-n-butylideneacetone oxide (IV). A mixture of 17 g of trans-n-butylideneacetone oxide and 200 ml of 0.5% sulfuric acid was refluxed for 5.5 hours (until the iodine ceased to be liberated after addition of potassium iodide to a test sample – a test for α-keto oxide). Then the diketone was steam distilled from the reaction mixture. After the distillation of ⅓ of the original volume, the steam distillation was stopped (the distillate began to run colorless). The distillate was saturated with table salt, extracted with ether, dried with sodium sulfate and vacuum distilled, after the distillation of the ether. 8.7 g (51%) of acetylvaleryl was isolated (2,3-heptanedione) (XIII) in the form of an oily liquid with yellow-green color and a characteristic sharp odor similar to that of diacetyl.

B.p. 35-35.5° (6 mm), 143-145° (743 mm), d^{20}_4 0.9241, $n^{20}D$ 1.4138.

Found %: C 65.54, 65.78; H 9.49, 9.45. $C_7H_{12}O_2$. Calculated %: C 65.62; H 9.38.

Bis-2,4-dinitrophenylhydrazone – crumbly, needle-shaped crystals with bright orange color and m.p. 210-211° (from a mixture of ethanol and ethyl acetate).

Found %: N 23.07, 22.98. $C_{19}H_{20}O_8N_8$. Calculated %: N 22.93.

The α-diketone is poorly soluble in water and changes on standing in air (shows an acid reaction).

Cleavage of the diketone (XIII). 4.2 g of the diketone and 10 ml of water were placed in a small flask and to the resulting mixture was added, in 3-4 portions with shaking, 7.5 ml of 27% hydrogen-peroxide solution and 3.6 g of sodium hydroxide in 20 ml of water. The yellow color of the solution and the characteristic odor of the diketone disappeared completely after the addition of the oxidizing agent. The solution was kept for two hours at room temperature, after which it was heated on a water bath for 20-25 minutes at 55-60°. Then, the solution was cooled, the neutral products were extracted with ether and the aqueous residue was evaporated nearly to dryness on a water bath. The resulting salts were decomposed with 10% sulfuric acid (until acid to Congo red), the resulting organic acids were extracted three times with ether, the extract was dried over sodium sulfate and distilled. 1.4 g of n-valeric acid was obtained (b.p. 183-185°, $n^{19}D$ 1.4080).

Found M 103, 99.8. $C_5H_{10}O_2$. Calculated M 102.

Simultaneously, about 1 g of acetic acid was isolated in the same experiment (b.p. 116-118°, $n^{20}D$ 1.3715, d^{20}_4 1.05).

Isolation of keto glycol – 3,4-dihydroxy-2-heptanone (XIV). The flask residue, after the distillation of the diketone (XIII) with steam, was saturated with potassium carbonate, the separated organic layer was removed and the aqueous layer was thoroughly extracted with ether. The separated layer and the ethereal extracts were combined, dried with roasted potassium carbonate and distilled under vacuum, after the ether had been distilled off. 6.5 g of 3,4-dihydroxy-2-heptanone was isolated in the form of a nearly colorless, viscous liquid, which was odorless.

B.p. 90° (1 mm), d^{20}_4 1.0613, $n^{20}D$ 1.4550, MR_D 37.29; calc. 37.58.

Found %: C 57.73, 57.39; H 9.44, 9.85; OH 23.76, 23.66. $C_7H_{14}O_3$. Calculated %: C 57.53; H 9.59; OH 23.29.

The 2,4-dinitrophenylhydrazone – small orange crystals with m.p. 214-215° (from a mixture of ethanol and ethyl acetate).

Found %: N 17.71, 17.62. $C_{13}H_{18}O_6N_4$. Calculated %: N 17.18.

The keto glycol is readily soluble in water, alcohol, benzene, acetone, and ether; less readily soluble in petroleum ether. It crystallized on standing into needle-shaped crystals with m.p. 30-32°.

Acetylation of keto glycol (XIV). Two or three drops of concentrated sulfuric acid was added to a solution of 4.8 g of the keto glycol in 50 g of freshly distilled acetic anhydride and the solution was heated under a reflux condenser on a steam bath for 10.5 hours. The reaction product was poured into 75-80 ml of ice water, the acetic acid was carefully neutralized with alkali, and with sodium carbonate near the end, the resulting acetate was extracted with ether, dried with sodium sulfate and vacuum distilled. 3 g of keto glycol diacetate was obtained in the form of a viscous, colorless liquid with a feeble odor.

B.p. 106-108° (1 mm), d^{20}_4 1.033, $n^{20}D$ 1.4360, MR_D 56.48; calc. 56.32.

Found %: C 57.26, 57.20; H 8.12, 8.10; CH_3CO 38.23, 37.66. $C_7H_{12}O_3(COCH_3)_2$. Calculated %: C 57.35; H 7.83; $COCH_3$ 37.39.

4. Oxidation of Trans-Isobutylideneacetone (I, R=iso-C_3H_7)

57 g of trans-isobutylideneacetone (b.p. 63-65° at 20 mm, $n^{20}D$ 1.4402, d^{20}_4 0.8409), prepared by the condensation of isobutyraldehyde with acetone [22], was placed in a three-necked flask with 200 ml of methanol and 100 ml of 18% of hydrogen-peroxide solution and 18 ml of 4-N aqueous sodium-hydroxide solution were added to the resulting solution with energetic stirring over 1 hour and 40 minutes at −10 to −11°. The mixture was stirred for about two hours longer at room temperature, after the addition of the entire amount of the oxidizing agent. 31 g (47%) of 2-methyl-3,4-epoxy-5-hexanone (V) was isolated after the usual treatment and vacuum distillation; this formed a colorless, mobile liquid with a pleasant, characteristic odor.

B.p. 54-55° (9 mm), d^{20}_4 0.9589, $n^{20}D$ 1.4275, MR_D 34.31; calc. 34.68. λ_{max} 290 mμ (in alcohol).

Found %: C 65.71, 65.65; H 9.28, 9.34. M 127.8, 130.4. $C_7H_{12}O_2$. Calculated %: C 65.62; H 9.38. M 128.0.

The 2,4-dinitrophenylhydrazone – dark yellow crystals with m.p. 141° (from alcohol).

Found %: N 18.24, 18.07. $C_{13}H_{16}O_5N_4$. Calculated %: N 18.18.

The keto oxide was difficultly soluble in water, readily soluble in the usual organic solvents. It displays an acid reaction after prolonged standing.

Hydrolysis and isomerization of the keto oxide (V). A mixture of 23 g of keto oxide (V) and 200 ml of 0.5% sulfuric acid was refluxed in a round-bottomed flask for 16 hours. 7 g of acetylisovaleryl was obtained (2-methyl-4,5-hexanedione) (XV) in the form of an oily liquid with yellow-green color and a penetrating odor [7, 8, 12].

B.p. 137-138°, d^{20}_4 0.9098, $n^{20}D$ 1.4148, MR_D 35.18; calc. 34.55.

Found %: C 65.32; H 9.34. M 126.9, 129. $C_7H_{12}O_2$. Calculated %: C 65.62; H 9.38. M 128.

Dioxime, m.p. 168° (from aqueous alcohol) [7, 8]; bis-2,4-dinitrophenylhydrazone, m.p. 222° (from alcohol).

Found %: N 23.17, 23.07. $C_{19}H_{20}O_8N_8$. Calculated %: N 22.95.

Keto glycol – 2-methyl-3,4-dihydroxy-5-hexanone (XVI). 4 g of the keto glycol (XVI) was isolated from the solution after the steam distillation of the diketone (see experiment above); this was a viscous liquid with yellowish color and a weak odor.

B.p. 84-85° (2.5 mm), d^{20}_4 1.0332, $n^{20}D$ 1.4552, MR_D 37.82; calc. 38.35.

Found %: C 57.47, 57.58; H 9.48, 9.55; OH 23.04, 22.97. M 148.2, 144.5. $C_7H_{14}O_3$. Calculated %: C 57.53; H 9.59; OH 23.29. M 146.

2,4-Dinitrophenylhydrazone – small, deep red crystals with m.p. 210° (from alcohol).

Found %: N 17.41. $C_{13}H_{18}O_6N_4$. Calculated %: N 17.18.

The keto glycol is rather readily soluble in water, soluble in the usual organic solvents.

5. Oxidation of Isoamylideneacetone (I, R=iso-C_4H_9)

The isoamylideneacetone used for the oxidation was prepared by the condensation of isovaleraldehyde with acetone in an alkaline medium [23]. The keto alcohol was the main reaction product, which was dehydrated by us into the isoamylideneacetone by vacuum distillation in the presence of concentrated sulfuric acid. 215 g (83%) of pure isoamylideneacetone with b.p. 64.5-65° (10 mm), $n^{20}D$ 1.4430, was obtained from 312 g of the keto alcohol after a vacuum distillation (15 mm) in the presence of 8-10 drops of concentrated sulfuric acid.

126 g of isoamylideneacetone, diluted with 500 ml of methanol, was oxidized by the addition of 200 ml of 18% hydrogen-peroxide solution and 17 ml of 4-N aqueous sodium-hydroxide solution over two hours at −8 to −10° with energetic stirring. After the mixture had been stirred for one hour longer and the usual treatment (methanol was distilled off in vacuum), there was isolated 107 g (75.7%) of isoamylideneacetone oxide (6-methyl-3,4-epoxy-2-heptanone) (VI) in the form of a colorless, mobile liquid with a pleasant odor.

B.p. 57° (1 mm), 84° (15 mm), d^{20}_4 0.9317, $n^{20}D$ 1.4303. MR_D 39.39; calc. 39.30. λ_{max} 285 mμ (in alc.).

Found %: C 67.79; H 9.78. M 140.2, 143.2. $C_8H_{14}O_2$. Calculated %: C 67.60; H 9.86. M 142.

The 2,4-dinitrophenylhydrazone – characteristic crumbly crystals with golden-yellow color and m.p. 135-136° (from alcohol).

Found %: N 17.05, 17.21. $C_{14}H_{18}O_5N_4$. Calculated %: N 17.39.

The keto oxide is difficultly soluble in water, readily soluble in the usual organic solvents. It is stable in storage.

Hydrolysis and isomerization of isoamylideneacetone oxide (VI). a) A mixture of 32 g of the keto oxide and 250 ml of 0.25% sulfuric acid was refluxed in a flask for 32 hours. Almost all the keto oxide passed into solution. The solution was saturated with potassium carbonate, the separated organic layer was removed, the aqueous portion was extracted three times with ether, the extract was combined with the separated layer, dried with potassium carbonate and distilled under vacuum, after the ether had been distilled off. 7 g of acetylisocaproyl (2-methyl-5,6-heptanedione) (XVIII) was isolated in the form of a yellow-green oil with a penetrating, characteristic odor of an α-diketone [7].

B.p. 39° (1 mm), 162-164° (752 mm), d^{20}_4 0.9212, $n^{20}D$ 1.4240, MR_D 39.31; calc. 39.17.

Dioxime – thin, needle-shaped crystals with m.p. 172-173° (from alcohol). Bis-2,4-dinitrophenylhydrazone – small orange crystals with m.p. 224-226° (after washing with methanol).

Found %: N 22.07, 22.40. $C_{20}H_{22}O_8N_8$. Calculated %: N 22.31.

2.5 g of keto glycol (2-methyl-4,5-dihydroxy-6-heptanone) (XVII) was isolated along with the dione (XVIII) in this experiment; the product had b.p. 85-86° (1 mm) and crystallized completely after a brief standing, yielding the characteristic long, needle-shaped crystals with m.p. 65-67° (from petroleum ether).

Found %: C 59.89, 59.72; H 10.08, 10.01; OH 21.92, 21.84. M 162.2, 159.8. $C_8H_{16}O_3$. Calculated %: C 60.00; H 10.00; OH 21.25. M 160.

2,4-Dinitrophenylhydrazone – orange crystals with m.p. 216-218° (after being washed on the filter with methanol).

Found %: N 17.08, 17.04. $C_{14}H_{20}O_6N_4$. Calculated %: N 16.47.

The keto glycol is soluble in alcohol, benzene and ether.

b) 15 g of the keto oxide and 200 ml of 2.5% sulfuric acid were refluxed in a flask for two hours. The upper layer was separated, the residue was evaporated under vacuum, saturated with potassium carbonate and extracted with ether. The separated layer and the ethereal extracts were combined, dried with potassium carbonate and vacuum distilled. 1.5 g of the original keto oxide (VI) and 6.5 g of the keto glycol (XVII) were isolated.

c) 17 g of the keto oxide and 250 ml of water were refluxed in a flask for 38 hours. After the usual treatment, 10 g of the original keto oxide and 1.5 g of the keto glycol (XVII) were isolated.

6. Oxidation of 3-Methyl-3-hepten-2-one (VII)

35 g of 3-methyl-3-hepten-2-one (VII) (b.p. 84-85° at 20 mm, $n^{19}D$ 1.4465) was placed in a three-necked flask with 220 ml of methanol; the starting ketone had been prepared by condensation of n-butyraldehyde with methylethyl ketone [24]. To the solution, cooled to −4°, there were simultaneously added, over 1 hour and 15 minutes with energetic stirring, 65 ml of 18% hydrogen-peroxide solution and 13.5 ml of 4-N sodium-hydroxide solution. The mixture was stirred with cooling for three hours and was set aside for twelve hours at room temperature. Then, 65 ml of 18% hydrogen-peroxide and 11.5 ml of 4-N sodium-hydroxide solution were added additionally to the reaction mixture. 9.4 g of hydrogen peroxide had reacted over three hours, this amount corresponding to the amount required by a calculation. After the usual treatment (methanol was distilled under vacuum of 110-115 mm), we obtained 20.3 g (51.4%) of 3-methyl-3,4-epoxy-2-heptanone (VIII) in the form of a colorless, mobile liquid with a characteristic pleasant odor.

B.p. 51-52° (4 mm), d^{20}_4 0.9298, $n^{20}D$ 1.4325, MR_D 39.68; calc. 39.30. λ_{max} 290 mμ (in alcohol).

Found %: C 68.10, 68.09; H 10.18, 10.15. M 142.4, 142.5. $C_8H_{14}O_2$. Calculated %: C 67.60; H 9.86. M 142.0.

2,4-Dinitrophenylhydrazone – bright orange crystals with m.p. 110° (from alcohol).

Found %: N 17.65, 17.69. $C_{14}H_{18}O_5N_4$. Calculated %: N 17.39.

The keto oxide was poorly soluble in water, readily soluble in the usual organic solvents.

Isomerization of 3-methyl-3-hepten-2-one oxide (VIII). A mixture of 16 g of the keto oxide and 170 ml of 2% sulfuric acid was refluxed for 20 hours. The isomerization began after two hours of boiling, and was accompanied by a change of color of the reaction mixture. 3 g of the α-diketone – 4-methyl-2,3-heptanedione (XIX) was isolated after the usual treatment and a vacuum distillation; this was in the form of a yellow-green oil with a characteristic penetrating odor.

B.p. 46-48° (5 mm), d^{20}_4 0.9159, $n^{20}D$ 1.4298, MR_D 40.00; calc. 39.17.

Found %: C 67.01; H 9.35. $C_8H_{14}O_2$. Calculated %: C 67.60; H 9.86.

The diketone was poorly soluble in water, soluble in the usual organic solvents.

Bis-2,4-dinitrophenylhydrazone – orange, needle-shaped crystals with m.p. 224-226° (from a mixture of ethanol and ethyl acetate).

Found %: N 21.74. $C_{20}H_{22}O_8N_8$. Calculated %: N 22.31.

For the proof of structure of the keto-group locations, the diketone (XIX) was subjected to cleavage with excess alkaline hydrogen peroxide. 3 ml of 27% hydrogen-peroxide solution and 1.3 g of sodium hydroxide in 6 ml of water were added, with shaking and water cooling, to 1.6 g of the diketone mixed with 5 ml of water and the decolorized solution was set aside for 2-3 hours at room temperature, after which it was heated under a reflux condenser for 25-30 minutes on a water bath. Then, the aqueous solution was evaporated on a water bath to a paste, acidified with 10% sulfuric acid to an acid reaction, the organic acids were extracted with ether and dried with sodium sulfate. The residue after the distillation of ether was heated with calcined lime in a test-tube partly stoppered with a piece of filter paper moistened with o-nitrobenzaldehyde solution [25]. The paper acquired a blue color (formation of indigo) under the action of acetone vapors, which indicated the presence of acetic acid. Since the other homologs of acetic acid do not give this reaction, while alkaline hydrogen peroxide cleaves the C–C bond of α-diketones between carbon atoms which carry the carbonyl oxygens [4], it follows that the presence of carbonyl groups in 2,3-positions of the diketone should be admitted.

7. Oxidation of 1-Methoxy-5-methyl-4-octen-3-one (IX)

64 g of freshly distilled 1-methoxy-5-methyl-4-octen-3-one (b.p. 84-86° at 3 mm, $n^{19}D$ 1.4550) [26] in 350 ml of methanol was oxidized over 45 hours with energetic stirring at 20° with 156 ml of 18% hydrogen-peroxide solution and 36 ml of 4-N sodium-hydroxide solution. 42.5 g (60%) of 1-methoxy-5-methyl-4,5-epoxy-3-octanone (X) was isolated in the form of a colorless, rather mobile liquid with a weak, characteristic odor.

B.p. 93-94° (1 mm), d^{20}_4 0.9754, $n^{20}D$ 1.4420, MR_D 50.50; calc. 50.18.

Found %: C 64.70; H 9.69. M 185,187. $C_{10}H_{18}O_3$. Calculated %: C 64.52; H 9.68. M 186.

2,4-Dinitrophenylhydrazone – bright yellow needles with m.p. 215° (from alcohol).

Found %: N 15.40, 15.43. $C_{16}H_{22}O_6N_4$. Calculated %: N 15.30.

The keto oxide was soluble in water (1:10), and readily soluble in the usual organic solvents.

8. Oxidation of 5-Methyl-1,4-octadien-3-one (XI)

40 ml of 18% hydrogen-peroxide solution and 8 ml of 4-N sodium-hydroxide solution were added, with energetic stirring at 20°, to a solution of 10.7 g of 5-methyl-1,4-octadien-3-one (b.p. 59-61° at 2 mm, $n^{18}D$ 1.4760) [2, 27] and 60 ml of dioxane placed in a small, three-necked flask. Then the solution was stirred for two hours more at this temperature. After the usual treatment (see above) and a vacuum distillation, 8.2 g (62%) of 5-methyl-1,2,4,5-diepoxy-3-octanone (XII) was isolated in the form of a colorless liquid with a weak, characteristic odor.

B.p. 84.5-85.5° (1 mm), d^{20}_4 1.0074, $n^{20}D$ 1.4570, MR_D 43.32; calc. 42.66.

Found %: C 63.21, 63.17; H 8.78, 8.85. M 169, 172. $C_9H_{14}O_3$. Calculated %: C 63.53; H 8.24. M 170.

2,4-Dinitrophenylhydrazone – bright yellow needles with m.p. 193-195° (from ethanol).

Found %: N 16.37, 16.29. $C_{15}H_{18}O_6N_4$. Calculated %: N 16.00.

The keto oxide is soluble in water and readily soluble in the usual organic solvents.

SUMMARY

1. The reaction of oxidation of a series of α,β-unsaturated ketones and 5-methyl-1,4-octadien-3-one with alkaline hydrogen peroxide was studied. Oxides of ethylideneacetone, propylideneacetone, trans-n- and trans-iso-butylideneacetones, isoamylideneacetone, 3-methyl-3-hepten-2-one, 1-methoxy-5-methyl-4-octen-3-one and 5-methyl-1,4-octadien-3-one were prepared and characterized for the first time.

2. It was shown that these oxides of alkylideneacetones and 3-methyl-3-hepten-2-one oxide isomerize into α-diketones under the influence of dilute sulfuric-acid solutions and hydrolyze at the same time into the corresponding keto glycols.

3. The ultraviolet absorption spectra of ethylideneacetone, propylideneacetone, trans-n- and trans-iso-butylideneacetone, isoamylideneacetone and 3-methyl-3-hepten-2-one were examined in the region of 200 to 400 mμ. It was established that they all possess an absorption band at 285-290 mμ which is related to the carbonyl group.

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SYNTHESIS AND HYDROGENATION OF 1,4,7-TRIPHENYLHEPTANE, 1,7-DIPHENYL-4-BENZYLHEPTANE AND 1,7-DIPHENYL-4-(2-PHENYLETHYL)-HEPTANE. III.

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In the present investigation we have continued the synthesis of triphenyl- and tricyclohexylcycloalkanes [1, 2]. The hydrocarbons were synthesized by the following general scheme:

$$C_6H_5{-}C{\equiv}C{-}CMgBr + C_2H_5OOC(C)_n{-}C_6H_5 \longrightarrow$$

$$(C_6H_5{-}C{\equiv}C{-}C)_2{-}C(OH){-}(C)_n{-}C_6H_5 \xrightarrow{-H_2O} \text{Olefin mixture}$$

$$\xrightarrow{+H_2} C_6H_5{-}C{-}C{-}C(C_6H_5){-}(C)_n{-}C{-}C{-}C{-}C_6H_5 \xrightarrow{+9H_2} C_6H_{11}C{-}C{-}C(C_6H_{11}){-}(C_n){-}C{-}C{-}C{-}C_6H_4$$

where n = 0, 1, 2.

The physicochemical properties of the resulting hydrocarbons are given in Table 1. The melting points (or freezing points) and the viscosities of hydrocarbons prepared in the present work and of those synthesized previously and differing only by the different disposition of phenyl and cyclohexyl rings in the alkane chain, are given in Table 2.

A comparison of the melting (or freezing) points and of viscosity indicates that the transition from triphenyl- and tricyclohexylalkanes, in which all rings are at the same carbon atom, to triphenyl- and tricyclohexylalkanes of the same molecular weight, but having a different disposition of the rings along the chain, causes a severe drop of the freezing points and viscosity indexes.

It was also interesting to compare the freezing points (and viscosities) of the triphenyl- and tricyclohexylalkanes synthesized by us. We can see that the freezing points drop from −15 to −38° with the growth of the length of the central side-chain, despite the increase of the molecular weight. (This interesting phenomenon had been noted earlier in the examples of aliphatic hydrocarbons.)

EXPERIMENTAL*

1,4,7-Triphenylheptane (I). One of the starting materials – 1-bromo-3-phenylpropane was prepared by us, following the technique of [3], in 75% yield, by a slow distillation of 1-phenyl-3-propanol with 48% hydrobromic acid.

B.p. 117° (25 mm), d^{20}_4 1.3057, $n^{20}D$ 1.5430, MR_D 48.04; calc. 47.94. Literature data [3]: b.p. 118-119° (17 mm).

*V.P. Khrukhtanova participated in the experimental work.

TABLE 1

Physicochemical Properties of Triphenyl- and Tricyclohexylalkanes

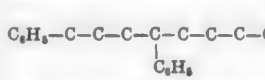
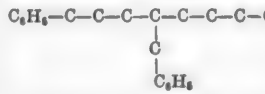
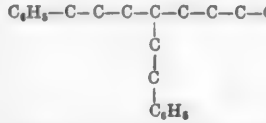
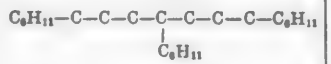
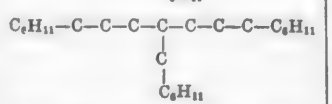
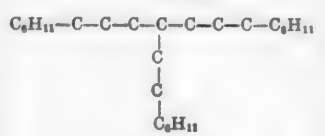
Compound No.	Structural formula	B.p. (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		Found (%)		Empirical formula	Calculated (%)	
					found	calc.	C	H		C	H
(I)		205° (0.5)	1.0013	1.5650	106.80	106.85	91.63, 91.52	8.26, 8.17	$C_{25}H_{28}$	91.38	8.62
(II)		233 (3)	1.0003	1.5650	114.47	114.46	91.13, 91.11	8.57, 8.73	$C_{26}H_{30}$	91.15	8.85
(III)		202—203 (1)	0.9924	1.5570	115.85	116.08	90.69, 90.74	9.09, 9.11	$C_{27}H_{32}$	90.94	9.06
(IV)		202 (2.5)	0.9088	1.4919	110.60	111.05	86.75, 86.52	13.42, 13.34	$C_{25}H_{46}$	86.56	13.42
(V)		237 (4)	0.9043	1.4910	115.46	115.67	86.64, 86.43	13.41, 13.31	$C_{26}H_{48}$	86.54	13.46
(VI)		214 (1) 220 (2)	0.9005	1.4900	120.24	120.29	86.34, 86.40	13.37, 13.47	$C_{27}H_{50}$	86.51	13.49

TABLE 2

Freezing Points (Melting Points) and Viscous Properties of Triphenyl- and Tricyclohexylalkanes

Compound no.	Empirical formula	Structural formula	Melting (freezing) point	Viscosity (in centistokes)			
				20°	50°	100°	150°
—	—	C_6H_5 / C_6H_5—C—(C)$_6$ / C_6H_5	76–76.5°	—	—	6.05	2.30
(I)	$C_{25}H_{28}$	C_6H_5–C–C–C–C–C–C–C–C–C_6H_5 (C$_6$H$_5$ on C4)	—15	97.8	20.5	5.45	1.65
—	—	C_6H_5 / C_6H_5—C—(C)$_7$ / C_6H_5	+5	—	572.0	15.0	3.65
(II)	$C_{26}H_{30}$	C_6H_5–C–C–C–C–C–C–C–C–C_6H_5 (C on C4; C$_6$H$_5$ on C)	—25	71.80	16.62	3.60	1.62
—	—	C_6H_5 / C_6H_5—C—C—(C)$_6$ / C_6H_5 / C	+15	—	422.0	15.82	4.88
(III)	$C_{27}H_{32}$	C_6H_5–C–C–C–C–C–C–C–C–C_6H_5 (C on C4; C on C; C$_6$H$_5$ on C)	—38	48.50	15.85	4.58	1.95
—	—	C_6H_{11} / C_6H_{11}—C—(C)$_6$ / C_6H_{11}	+10	—	635.0	19.40	3.21
(IV)	$C_{25}H_{46}$	C_6H_{11}–C–C–C–C–C–C–C–C–C_6H_{11} (C_6H_{11} on C4)	—20	423.19	49.37	6.80	2.38
—	—	C_6H_{11} / C_6H_{11}—C—C—(C)$_6$ / C_6H_{11} / C	+2	—	431.0	16.5	4.0
(VI)	$C_{27}H_{50}$	C_6H_{11}–C–C–C–C–C–C–C–C–C_6H_{11} (C on C4; C on C; C_6H_{11} on C)	—25	274.0	35.84	10.0	3.59

95 g (39%) of the product was obtained from 112 g of ethyl benzoate (b.p. 93° at 14 mm) and $C_6H_5CH_2$-CH_2CH_2MgBr (from 300 g of 1-bromo-3-phenylpropane): b.p. 208° (1 mm), d^{20}_4 1.0211, $n^{20}D$ 1.5825, MR_D 106.44; calculated 106.38; this product was an olefin mixture obtained by dehydration of the 1,4,7-triphenyl-4-heptanol in the process of the reaction and the subsequent treatment of the reaction mixture.

30 g of the olefin mixture was hydrogenated under hydrogen pressure over Raney nickel at 40°; 27 g of (I) was isolated. 11 g of olefin mixture was hydrogenated as indicated above at 170°; 8 g of 1,4,7-tricyclohexylheptane (IV) was isolated.

1,7-Diphenyl-4-benzylheptane (II). 105 g (44%) of a product which was a mixture of 1,7-diphenyl-4-benzyl-4-heptanol and the products of its dehydration, was obtained from 110 g of phenylacetic acid (b.p. 188° at 11 mm, d^{20}_4 1.0314, $n^{20}D$ 1.5020; in literature data [4]: b. p. 227° at 760 mm, d^{20}_4 1.0333, $n^{18.5}$ 1.4992) and $C_6H_5CH_2CH_2CH_2MgBr$ (from 300 g of 1-bromo-3-phenylpropane). The mixture was subjected to a complete dehydration by method [5]. The resulting olefin mixture had the following constants: b. p. 237° (3 mm), d^{20}_4 1.0097, $n^{20}D$ 1.5765, MR_D 111.62; calc. 111.0.

35 g of (II) was isolated by hydrogenation of 41 g of the mixture at 50° (conditions as indicated above). 18 g of 1,7-dicyclohexyl-4-(cyclohexylmethyl)-heptane (V) was obtained by hydrogenation of 23 g of the mixture at 170°.

1,7-Diphenyl-4-(2-phenylethyl)-heptane (III). 101 g (59%) of 1,7-diphenyl-4-(2-phenylethyl)-heptan-4-ol with m.p. 60-61° was obtained from 87 g of ethyl hydrocinnamate (b.p. 124° at 16 mm, $n^{20}D$ 1.4932; in the literature [6]: b.p. 122.8° at 12 mm, $n^{20}D$ 1.4954) and $C_6H_5CH_2CH_2CH_2MgBr$ (from 266 g of 1-bromo-3-phenylpropane).

Found %: C 87.07; H 8.51; OH 4.1. $C_{27}H_{32}O$. Calculated %: C 87.03; H 8.68; OH 5.0.

The dehydration was run as indicated previously [5]. A mixture of olefins amounting to 58 g (60%) was obtained after heating 100 g of the carbinol with 166 g of acetic acid and 1 ml of sulfuric acid (concentrated) for 30 minutes on a water bath:

B.p. 268° (5 mm), d^{20}_4 1.0036, $n^{20}D$ 1.5710, MR_D 115.85; calc. 115.62.

21 g of (III) was obtained by hydrogenation of 30 g of this mixture at 40°. 15 g of 1,7-dicyclohexyl-4-(2-cyclohexylethyl)-heptane (VI) was obtained by hydrogenation of 21 g of the mixture at 170°.

SUMMARY

1,4,7-Triphenylheptane, 1,7-diphenyl-4-benzylheptane, 1,7-diphenyl-4-(2-phenylethyl)-heptane, 1,4,7-tricyclohexylheptane, 1,7-dicyclohexyl-4-(cyclohexylmethyl)-heptane and 1,7-dicyclohexyl-4-(2-cyclohexylethyl)-heptane were synthesized for the first time and their freezing points and the viscosity properties at various temperatures were determined for these hydrocarbons.

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CATALYTIC HYDROGENATION OF VINYLACETYLENE FOR THE PREPARATION OF BUTADIENE

I. GENERAL KINETIC RULES OF SELECTIVE HYDROGENATION OF VINYLACETYLENE IN SOLUTION

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One of the possible methods of preparation of butadiene from acetylene is the dimerization of the latter into vinylacetylene with the subsequent hydrogenation of the latter to butadiene. The possibility, in principle, of production of butadiene by the catalytic hydrogenation of vinylacetylene was first established by S.V. Lebedev [1] and A.L. Klebanskii and co-workers [2]. Our study is directed to the detailed study of the process of catalytic hydrogenation of vinylacetylene for the purpose of raising the selectivity of the reaction. In addition, we also set up as our goal the theoretical development of the technological basis of this process for its industrial realization.

It was established as a result of the study of the composition of the products of the reaction of hydrogenation of vinylacetylene in solution with various catalysts that the most selective hydrogenation occurs in the presence of a palladium catalyst. The catalysts studied by us may be arranged in the following descending order of selectivity of action: palladium catalysts, Raney iron, Raney nickel, platinum black. The special selectivity of hydrogenation of certain acetylenic compounds in the presence of Raney iron catalyst indicated in the literature [3, 4] was not confirmed for the hydrogenation of vinylacetylene.

Running the hydrogenation of vinylacetylene in gas phase over a palladium catalyst at 130° failed to give the desired results. As in the work of previous authors [2, 5], the reaction proceeded unselectively and, even in the first stage of hydrogenation, yielded considerable amounts of butylenes, butane and liquid polymerization products of vinylacetylene, while the catalyst rapidly lost its activity. Dilution of vinylacetylene with water vapor failed to diminish the formation of the by-products. For this reason, all further work on hydrogenation of vinylacetylene was run by us in a glass vessel, capable of being rocked, in the presence of a palladium catalyst deposited on finely divided silica gel. In the initial stage of the process, the hydrogenation proceeds according to the reaction kinetics of zero order with respect to vinylacetylene and of first order with respect to hydrogen. In the kinetic region of hydrogenation, the reaction rate is directly proportional to the amount of the catalyst and does not depend on the intensity of agitation of the solution. In the diffusional region of the reaction with respect to hydrogen, the reaction rate is directly proportional to the intensity of agitation of the solution and does not depend on the amount of the catalyst. The reaction rate in both the kinetic and the diffusional regions of hydrogenation is directly proportional to the partial pressure of hydrogen. The apparent activation energy of the reaction in the kinetic region is equal to about 10,000 calories per gram-mole, and in the diffusional region with respect to hydrogen – about 5000 calories per gram-mole.

According to the literature data, during the hydrogenation of vinylacetylene in solution in the presence of a palladium catalyst [1, 2, 5] the further hydrogenation of butadiene and butylenes takes place along with the predominant addition of hydrogen to the acetylenic bond. In order to select the conditions which would assure the greatest selectivity of the process and which facilitate the isolation of the main reaction product – butadiene, in pure state, we carried out a study of the composition of the products formed at various degrees of hydrogenation.

Some data on the composition of the products of reaction after the addition of one or more gram-moles of hydrogen to one gram-mole of vinylacetylene exist in the studies cited in the literature. For this reason, we directed our principal attention to the study of the composition of the products obtained at low degree of hydrogenation. It was established that in the initial stage of the process and up to about 30% degree of hydrogenation (calculated on the acetylenic bond), the addition of hydrogen occurs mainly at the triple bond. During the further hydrogenation, the simultaneous hydrogenation of the resulting butadiene occurs along with the predominant addition of hydrogen to the acetylenic bond and the reaction products form a multicomponent, difficultly separable hydrocarbon mixture. The reaction character indicated above was confirmed by hydrogenation of a mixture of vinylacetylene and butadiene. The butadiene present in the initial mixture, as well as that formed in the course of the hydrogenation process, practically does not react until its total concentration in the solution reaches about 30%.

It was shown by this study that ethylacetylene is not formed in the hydrogenation of vinylacetylene and the data cited by S.V. Lebedev about the absence of methyl-allene in the reaction products [1] have been confirmed. Thus, it is possible to consider as proven, on the basis of the data secured by us, that the first hydrogen molecule adds to vinylacetylene exclusively in 1,2-position (at the triple bond) with formation of butadiene.

EXPERIMENTAL

The technique of running the experiments and preparation of catalyst. For the study of the process of vinylacetylene hydrogenation we used the apparatus suggested by S.V. Lebedev [6] in a simplified form; a rocking vessel, connected to two burettes for pumping air from the system and for supplying the hydrogen, was placed in a thermostat in which the desired temperature was maintained with accuracy of ±0.5°. Into the vessel we placed 1% aqueous palladium-chloride solution, finely divided silica gel and ethyl alcohol (95% concentration). After the reduction of palladium chloride with hydrogen, the predetermined amount of vinylacetylene was charged and its hydrogenation was run. Upon completion of hydrogenation the solution was transferred into a flask containing

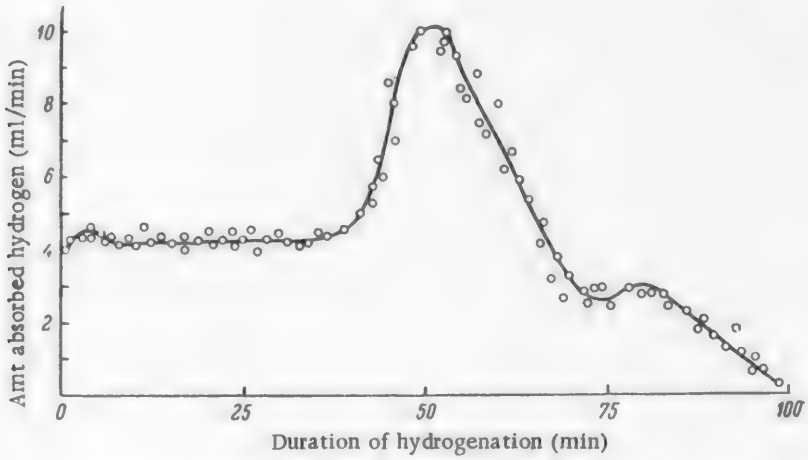

Fig. 1. Kinetic curve of hydrogenation of vinylacetylene in presence of palladium.

a saturated sodium-chloride solution and connected to a reflux condenser. The desorption was run by heating the solution to boiling. The liberated gas was collected in a gasometer. Air was blown through the solution, after cessation of gas evolution, for a more complete isolation of the reaction products. Hydrogenation of vinylacetylene under the laboratory conditions was run with hydrogen obtained by the action of 20% alkali solution on pure aluminum. The vinylacetylene was used after having been freshly redistilled through a Podbielniak column.

Analytical methods. The reaction products, after incomplete hydrogenation of vinylacetylene, are a complex mixture of substances, consisting of the initial vinylacetylene, butadiene, butylenes, butane and hydrogen.

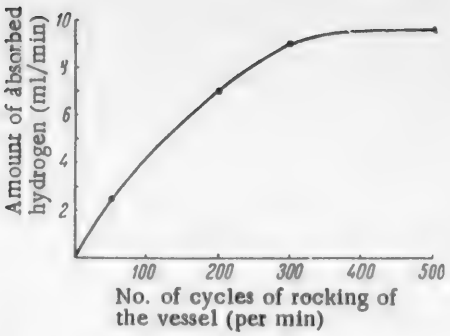

Fig. 2. Dependence of the hydrogenation rate on intensity of agitation.

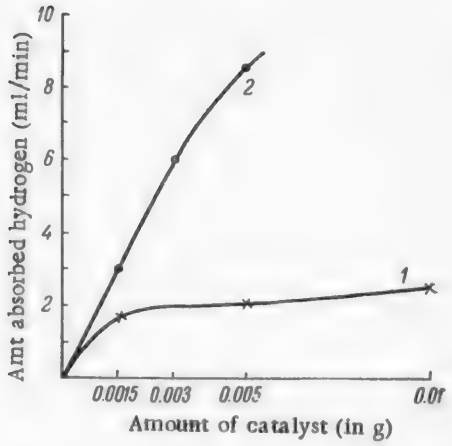

Fig. 3. Dependence of the rate of hydrogenation on the amount of the catalyst: 1) number of rocking cycles of vessel per minute – 60; 2) number of rocking cycles of vessel per minute – 300.

The most accurate among the tested methods for the determination of vinylacetylene (ammoniacal solution of silver nitrate; modified Chevastelon method [7, 8]) was the method of absorption of vinylacetylene by the alkaline solution of mercury cyanide. After the absorption of vinylacetylene, the total amount of unsaturated compounds (butadiene and butylenes) in the residual gas was determined by their absorption by an aqueous solution of bromine. Butane and hydrogen were determined by combustion over cupric oxide. The butadiene determination was run on a separate sample of the gas, which had been first freed completely of vinylacetylene (by its being absorbed in an alkaline solution of mercury cyanide), the analysis being performed by the technique adopted by the synthetic rubber industry (bromination of the gas and calculation of the butadiene content from the weight of the resulting tetrabromide [9].

General kinetic rules of hydrogenation of vinylacetylene in solution are illustrated on Figs. 1-4. It is evident from the data given in Fig. 2, that with the rate of rocking of the apparatus vessel at more than 300 cycles per minute the kinetic region of the reaction is reached and the reaction rate remains constant. With the number of the rocking cycles of the vessel ranging from about 200-300 per minute, the reaction occurs in the diffusionally kinetic region. At greater intensity of agitation (about 300 rocking cycles of the vessel per min) the rectilinear dependence of the hydrogenation rate and the amount of the catalyst, which corresponds to the kinetic region of hydrogenation is maintained over the entire interval of alteration of the amount of the catalyst studied by us (Fig. 3). At a low rate of agitation (about 60 rocking cycles of the vessel per minute), the rectilinear relationship between the hydrogenation rate and the amount of the catalyst is observed for only very small amounts of the catalyst. With increase of the catalyst amount to 0.005 g, the reaction rate reaches its limiting maximum value and the hydrogenation process passes from the kinetic region to the diffusional one.*

Determination of ethylacetylene and methylallene in the hydrogenation products of vinylacetylene. It is possible to admit the formation of ethylacetylene by the addition of hydrogen to the double bond in the process of vinylacetylene hydrogenation and that of methylallene if the addition of hydrogen occurs in 1,4-position. Ethylacetylene, in case of its presence among the reaction products, should be determinable along with vinylacetylene during the absorption with alkaline solution of mercury cyanide, while methylallene should be determined along with butadiene as the corresponding bromides. For analysis of ethylacetylene and methylallene we used the method of determination of hydrogen numbers of the products of partial hydrogenation of vinylacetylene of known composition. The determination of the hydrogen numbers was run by hydrogenation in the presence of platinum in alcoholic solution. For the determination of ethylacetylene, the acetylenic compounds were first isolated from the products of partial hydrogenation of vinylacetylene by their being absorbed in an ammoniacal silver-nitrate solution. The silver derivatives were then decomposed with 10% hydrochloric-acid solution. Part of the resulting product was analyzed for the content of acetylenic compounds by means of an alkaline solution of mercury cyanide. The other part of the sample was exhaustively hydrogenated in the presence of a platinum catalyst and the presence of ethylacetylene could be judged by the consumption of hydrogen. The products of

*A more detailed account of the kinetic regularities of vinylacetylene hydrogenation in solution will be presented in another paper.

TABLE 1

Hydrogenation of Vinylacetylene in the Presence of Palladium Deposited on Silica Gel

Duration of hydrogenation (min)	Degree of hydrogenation (in %)	Comp. of reaction products (in volume %)				Losses (%)	Comp. of reaction products, with loss accounting (volume %)			
		vinyl-acetylene	buta-diene	butyl-enes	butane		vinyl-acetylene	buta-diene	butyl-enes	butane
25	31.4	60.7	26.0	None	None	13.3	68.6	31.4	None	None
30	39.8	57.1	37.5	»	»	5.4	60.2	39.8	»	»
40	57.4	46.2	40.2	6.7	»	6.9	49.6	43.0	7.4	»
45	60.3	44.1	37.9	8.6	»	9.4	49.1	41.5	9.4	»
50	63.0	43.9	43.0	8.1	»	5.0	45.9	45.2	8.9	»
70	73.5	37.4	40.6	13.6	»	8.4	41.2	44.2	14.7	»
100	115.9	10.6	58.0	25.8	»	5.6	11.4	61.3	27.3	»
110	126.3	7.1	53.5	31.6	»	7.8	7.7	58.3	34.0	»
120	147.1	3.4	50.1	45.0	1.3	0.2	3.4	50.2	45.1	1.3
150	162.2	3.5	31.7	58.5	2.5	3.8	3.5	33.2	60.8	2.5
200	206.0	Traces	Traces	88.1	5.6	6.3	None	None	94.0	6.0
220	212.5	None	»	81.9	11.6	6.5	»	»	87.5	12.5
290	218.0	»	»	75.6	16.4	8.0	»	»	82.0	18.0
360	292.1	»	»	7.7	90.8	1.5	»	»	7.9	92.1

partial hydrogenation of vinylacetylene indicated the absence of any ethylacetylene since the consumption of hydrogen corresponded exactly to the content of vinylacetylene. The products of partial hydrogenation of vinylacetylene were also used for the estimation of methylallene. After the separation of the acetylenic compounds with ammoniacal silver-nitrate solution in one gas sample, the butadiene content and the butylene content were determined by the bromination method. Butadiene was isolated in the form of its crystalline tetrabromide with m.p. 117° (m.p. of methylallene tetrabromide is 2°). Methylallene tetrabromide distills along with the bromides of the butylenes. Another part of the sample was hydrogenated over platinum. The hydrogen consumption corresponded precisely to the calculated amount of butadiene and butylenes from the analytical data. The hydrogen numbers should have been higher in the presence of noticeable amounts of methylallene. Thus, the first molecule of hydrogen adds only to the triple bond of vinylacetylene at 1,2-position, with formation of butadiene.

TABLE 2

Hydrogenation of Vinylacetylene in a Mixture with Butadiene

Composition of initial mixture		Duration of hydrogenation (in min)	Composition of reaction products (in volume %)		
vinyl-acetylene	butadiene		vinyl-acetylene	butadiene	butylenes
90	10	20	69.4	29.3	None
90	10	20	61.7	35.9	"
90	10	25	59.3	37.0	3.1
90	10	35	36.3	42.1	11.7
83	17	15	56.6	37.2	2.1
67	33	15	58.0	38.1	2.1

Composition of reaction products depending on the degree of hydrogenation. The experiments were run in the rocking vessel at 0° with about 300 rocking cycles of the apparatus per minute. 0.009 g of palladium (1.8 g of 1% aqueous palladium-chloride solution) was taken for each experiment along with 1 g of finely divided silica gel, 35 ml of 95% ethyl alcohol and 300-400 ml of gaseous vinylacetylene (about 0.75-1.0 g). The process was interrupted in each experiment after the absorption of a predetermined amount of hydrogen, in order to obtain the data for various degrees of the hydrogenation. The reaction products, isolated from the alcoholic solution, were analyzed for the content of vinylacetylene, butadiene, butylenes and butane. The results of the experiments are given in Table 1. According to the notation adopted by us, the addition of one molecule of hydrogen to one

molecule of vinylacetylene corresponds to 100% degree of hydrogenation. Losses of reaction products, by material balance, ran from 4% to 8% in most of the experiments.

The data in Table 1 are shown in Fig. 4 in the form of curves of change of vinylacetylene, butadiene, butylene and butane concentration during the hydrogenation process depending on the degree of conversion. The degree of conversion was calculated from the analysis of reaction products (with accounting for the losses). It is clear from the data in Fig. 4 that the maximum concentration of butadiene in the gas (50-60%) is reached at the addition of about 1 mole of hydrogen per one mole of vinylacetylene, while the content of vinylacetylene, as well as of butylenes, in the gas was 20-25% of each of these. The maximum yield of butadiene, based on the consumed vinylacetylene, may be attained at the degree of hydrogenation up to 30%; here, the reaction gas (the hydrogen not being considered) would consist of butadiene (up to 30%), original vinylacetylene (70%), and possibly small amounts of butylenes. The separation of butadiene from vinylacetylene, as shown by us, may be attained by the usual fractionation.

The data in Table 2 indicate that the butadiene contained in the original mixture, as well as that formed in the hydrogenation process, practically does not enter the reaction until its total concentration in the solution reaches about 30-35%.

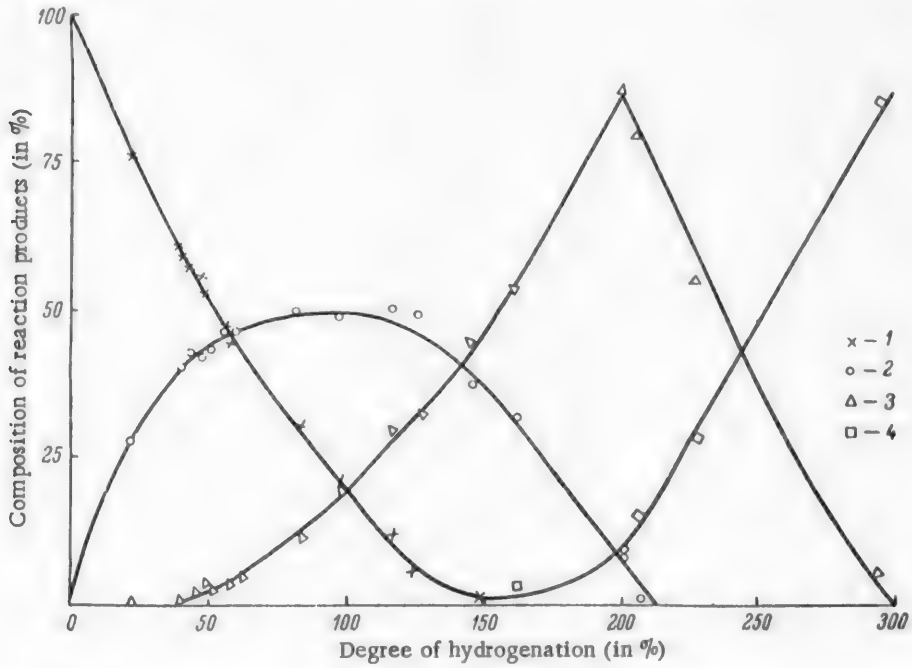

Fig. 4. Composition of products of hydrogenation of vinylacetylene in the presence of palladium deposited on silica gel, depending on the degree of hydrogenation: 1) vinylacetylene; 2) butadiene; 3) butylenes; 4) butane.

The characteristic changes in the kinetic curve may be explained by the comparison of Fig. 4 and the kinetic hydrogenation curve for vinylacetylene in Fig. 1. The transition from the horizontal region to the ascending branch of the kinetic curve corresponds to the maximum butadiene content in the reaction mixture, i.e., to the instant at which the hydrogenation of butadiene begins to predominate noticeably over the hydrogenation of vinylacetylene. The region of maximum rate on the kinetic curve corresponds to the hydrogenation of essentially butadiene. The maximum on the kinetic curve corresponds to the degree of hydrogenation of 160-170%. This degree of hydrogenation corresponds, according to the graph, to the following composition of reaction products: butadiene about 35%, vinylacetylene traces, butylenes about 65% and butane traces. The descending branch of the kinetic curve corresponds to hydrogenation of butylenes. The proximate composition of the butylenes formed in the hydrogenation process may be determined by the S.V. Lebedev rule. The relative content of β-butylene is determined as 30-35% from the second portion of the descending branch of the curve which corresponds to hydrogenation of this olefin.

SUMMARY

1. The possibility of selective hydrogenation of vinylacetylene over palladium catalyst in ethyl-alcohol solution with a low degree of hydrogenation (up to 30%) with formation of practically solely butadiene has been demonstrated.

2. The basic kinetic rules of hydrogenation of vinylacetylene in solution in the presence of a palladium catalyst were studied.

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CATALYTIC HYDROGENATION OF VINYLACETYLENE FOR THE PREPARATION OF BUTADIENE

II. EFFECT OF VARIOUS FACTORS ON THE RATE AND THE SELECTIVITY OF HYDROGENATION OF VINYLACETYLENE

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It was shown in the previous paper [1] that, during hydrogenation of vinylacetylene in ethyl-alcohol solution in the presence of palladium catalyst, the addition of hydrogen in the initial stage of the process, up to 30-35% degree of hydrogenation (calculated on the acetylenic bond), takes place practically exclusively at the triple bond with formation of butadiene.

In the present paper we present some data on the effect of the nature of the catalyst support and solvent, reaction temperature and intensity of stirring of the solution on the rate and the selectivity of the hydrogenation reaction of vinylacetylene.

In order to study the effect of conditions of the preparation of the catalyst and the character of the support on the rate and the selectivity of hydrogenation of vinylacetylene, we ran some studies with palladium precipitated on silica gel, barium sulfate and, as well, on polyvinyl alcohol. It was found that the alteration of the conditions of preparation of the catalyst and the character of the support affects the reaction rate but does not noticeably affect the selectivity of hydrogenation. The data obtained by us agree completely with the known studies of this problem [2].

The effect of the nature of the solvent on the rate of hydrogenation of acetylenic compounds in the presence of a palladium catalyst has been also noted in the literature [2, 3]. This effect is determined by the relative abilities of the solvents to be adsorbed by the catalyst as well as by the different solubilities of the substance being hydrogenated and of the hydrogen in them. It was proved by the studies run by us that hydrogenation of vinylacetylene proceeds at different rates in different solvents but with the same selectivity. Data on hydrogenation of vinylacetylene at different temperatures (from $-16°$ to $+20°$) showed a slight improvement of selectivity of the process with elevation of temperature. The established noticeable influence of intensity of stirring on reaction selectivity may be noted. In experiments run without stirring or with a very low stirring intensity (about 60 rocking cycles of the apparatus per minute), which correspond to the diffusional region of hydrogenation, the reaction proceeded unselectively. Even in the early stage of the process at hydrogenation level of 30%, approximately equal amounts of butadiene and butylenes were present in the reaction products. Hydrogenation of vinylacetylene in the kinetic region (about 500 rocking cycles of the apparatus per minute) and in the diffusional region relative to hydrogen only (about 200-300 cycles per minute) proceeds with the same selectivity.

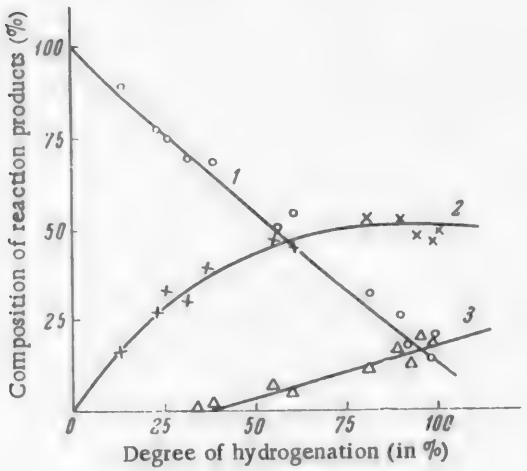
The established character of hydrogenation of vinylacetylene in solution in the presence of a palladium catalyst, as well as the relationship found between the selectivity of the process and the intensity of stirring of the solution, find a good explanation from the point of view of the adsorptional theory of catalytic hydrogenation [4].

The effect of the pH of the medium on the rate and the selectivity of the reaction was established with the study of the process of hydrogenation of vinylacetylene. The reaction proceeds at a greater rate in alcoholic solution with pH over 7, but this occurs with lower degree of selectivity than in acid or neutral medium.

An indication is found in the literature [5] that acetylenic compounds are less sensitive to the action of some inhibitors than are the corresponding ethylenic compounds. One might expect an improved selectivity of the process in the case of application of inhibiting substances which repress the secondary reaction to a greater degree than the first reaction in hydrogenation of vinylacetylene. However, during hydrogenation in the presence of hydrogen sulfide, as well as mercury and copper acetates, it was shown that even insignificant amounts of these substances poison the catalyst and greatly retard the reaction. The hydrogenation of vinylacetylene in the presence of these substances also proceeds less selectively; here the selectivity drops to a greater degree when the content of the inhibiting substances in solution is greater.

EXPERIMENTAL

In order to clarify the effect of the nature of the support on the rate and the selectivity of hydrogenation of vinylacetylene we ran a study with palladium precipitated on barium sulfate as well as on polyvinyl alcohol. The other conditions were the same as in running the experiments with palladium precipitated on silica gel [1]. The resulting data indicate the total analogy of the process of hydrogenation of vinylacetylene in all three cases. At the degree of hydrogenation up to 30% the addition of hydrogen proceeds practically solely at the acetylenic bond. Quite similarly proceeds the change of concentration of vinylacetylene, butadiene and butylenes depending on the degree of hydrogenation. Only the rate of hydrogenation is notably different, which is somewhat lower with palladium on barium sulfate and somewhat higher with palladium on polyvinyl alcohol, than with the catalyst precipitated on silica gel. The data about the reaction product composition after hydrogenation of vinylacetylene in the presence of palladium deposited on barium sulfate are shown in the figure. Similar data were obtained also with palladium on polyvinyl alcohol.



Composition of products of hydrogenation of vinylacetylene in the presence of palladium precipitated on barium sulfate depending on the degree of hydrogenation: 1) vinylacetylene; 2) butadiene; 3) butylenes.

In order to clarify the effect of the nature of the support on the process of hydrogenation of vinylacetylene, we tested the following solvents: ethyl alcohol, acetic acid, dioxane, methylcyclohexane, ethyl acetate, benzene, ethylbenzene, and xylene. The reaction was run at 0°. 0.009 g of palladium precipitated on 1 g of silica gel, 20 ml of solvent and 300-350 ml of gaseous vinylacetylene were taken for each experiment. The hydrogenation of vinylacetylene in the presence of ethylbenzene and xylene was run by the continuous method in an apparatus with a stirrer (Table 2).

It is evident from the data cited in Tables 1 and 2 that no principal difference is observed in the selectivity of the process. However, the use of different solvents is notably reflected in the hydrogenation rate. The reaction rate is approximately three times greater in the presence of ethylbenzene and xylene than with ethyl alcohol. The reaction rate declines by a factor of four in the presence of acetic acid and dioxane. The reaction proceeds most slowly in benzene solution, which may be explained by the possible presence of impurities (thiophene) in the benzene.

Hydrogenation of vinylacetylene with different intensities of stirring of the reaction mixture. In order to study the change of selectivity of hydrogenation of vinylacetylene during transition from the kinetic to the diffusional region, we determined the composition of the reaction products at various intensities of stirring (500, 300, 200 and 60 rocking cycles of the apparatus per minute) as well as without stirring of the solution. The degree of hydrogenation for all experiments was within the limits of 30-65%. 0.009 g of palladium, 1 g of silica gel, 35 ml of alcohol and 300-400 ml of vinylacetylene were used for each experiment. The experiments were run at 0°.

TABLE 1

Hydrogenation of Vinylacetylene in Various Solvents

Name of solvent	Duration of hydrogenation (min)	Degree of hydrogenation (%)	Composition of reaction products (in volume %)		
			vinylacetylene	butadiene	butylenes
Ethyl alcohol	50	31.4	68.6	31.4	None
Acetic acid	145	31.8	69.0	31.0	None
	180	62.3	47.2	43.3	9.5
	230	94.2	26.1	53.6	20.3
Dioxane	150	31.6	68.4	31.6	None
	160	47.5	59.8	32.9	7.3
Methylcyclohexane	50	25.0	75.0	25.0	None
	85	32.5	67.5	32.5	None
	105	49.5	54.3	41.9	3.8
Ethyl acetate	30	20.5	79.5	20.5	None
	30	27.3	72.7	27.3	None
	35	31.0	69.0	31.0	None
	60	86.5	34.0	45.5	20.5
Benzene	270	49.4	56.0	38.6	5.4
	315	67.8	46.1	40.0	13.9

TABLE 2

Hydrogenation of Vinylacetylene in the Presence of Ethylbenzene and Xylene

Name of solvent	Ratio of hydrogen to vinylacetylene	Feed rate of gaseous mixture (liters per hr per liter of catalyst)	Degree of hydrogenation (%)	Composition of reaction products (in volume %)		
				vinylacetylene	butadiene	butylenes
Ethyl alcohol	0.9 : 1	32	29.9	70.7	28.7	0.6
Xylene	0.9 : 1	50	61.6	46.9	42.2	9.7
	0.9 : 1	86	51.0	54.2	36.4	7.3
	0.9 : 1	93	45.4	58.2	35.3	5.1
	1.1 : 1	91	51.0	52.5	40.0	5.5
Ethylbenzene	1.1 : 1	56	83.3	24.7	56.7	13.3
	1.1 : 1	58	70.6	36.6	51.4	9.6

TABLE 3

Hydrogenation of Vinylacetylene with Various Intensities of Stirring of the Solution

Duration of hydrogenation (min)	No. of rocking cycles of apparatus (per min)	Degree of hydrogenation (%)	Composition of reaction products (in volume %)			
			vinylacetylene	butadiene	butylenes	losses, from material balance (%)
30	200	37.0	62.0	36.5	None	1.5
29	300	32.1	67.1	31.7	None	1.2
20	500	33.7	65.1	33.1	None	1.8
20	500	37.2	60.0	35.4	None	4.6
40	60	41.6	64.6	24.3	7.9	3.2
45	60	42.0	62.2	27.5	6.4	3.3
55	60	68.0	47.6	37.3	13.6	4.5
58	60	68.2	47.0	37.3	14.3	1.4
410	Without stirring	32.0	75.5	8.2	10.9	5.4
630	The same	33.6	77.5	10.8	11.4	0.3

TABLE 4

Hydrogenation of Vinylacetylene at Various Values of pH of Alcoholic Solution

pH of solution	Duration of hydrogenation (min)	Degree of hydrogenation (%)	Comp. of reaction products (volume %)			Remarks
			vinylacetylene	butadiene	butylenes	
1.4	30	34.4	65.6	34.4	None	Palladium on silica gel
5.0	30	34.6	65.4	34.6	None	
8.0	25	45.8	66.8	20.6	12.6	
10.0	20	45.7	66.2	21.9	11.9	
12.5	20	46.6	65.2	22.4	12.1	
14.0	15	43.1	68.2	20.5	11.3	
7.5	80	31.8	68.2	31.8	None	Palladium on barium sulfate
12.5	65	34.1	71.2	23.5	5.3	
14.0	65	45.7	69.0	16.3	14.7	
1.4	240	28.4	71.6	28.4	None	Palladium without support
14.0	90	43.6	69.5	17.4	13.1	

TABLE 5

Hydrogenation of Vinylacetylene in the Presence of Substances Which Retard the Reaction

Name of substance	Amt of substance (in % relative to palladium)	Duration of expt. (min)	Comp. of reaction products (volume %)			Losses, from material balance (%)
			vinylacetylene	butadiene	butylenes	
Without addend	—	110	55.2	37.1	5.5	2.2
Mercury acetate	$3.2 \cdot 10^{-4}$	220	59.1	31.5	6.9	2.5
	$3.2 \cdot 10^{-2}$	255	63.6	21.5	9.7	5.2
Copper acetate	$0.2 \cdot 10^{-4}$	135	51.5	33.8	11.9	3.1
	$2.5 \cdot 10^{-1}$	600	73.2	22.7		4.1*
Hydrogen sulfide	$2.7 \cdot 10^{-10}$	335	54.0	26.1	9.5	10.4
	$2.7 \cdot 10^{-5}$	765	77.1	21.3		1.6*

It is evident from the data in Table 3 that the selectivity of the process remained the same with alteration of the intensity of stirring within the limits of 200-500 rocking cycles of the apparatus per minute. With the degree of hydrogenation being 30-35%, the formation of practically only butadiene occurs. In experiments without stirring, the reaction proceeded unselectively. At 30% degree of hydrogenation, the reaction products contained equal amounts of butadiene and butylenes: 8.2 and 10.9%, respectively, in one experiment and 10.8 and 11.4% in another. The selectivity of hydrogenation in experiments run with 60 rocking cycles per minute was intermediate between the results of experiments with greater intensity of stirring and those without stirring. Thus, with 40% degree of hydrogenation, the concentration of butylenes in the reaction products reached 6-7% with the butadiene concentration of but only about 25%. The hydrogenation in this case proceeded in the diffusional region not only in respect to hydrogen but also in respect to the unsaturated compounds.

Effect of pH of the medium on the rate and the selectivity of hydrogenation of vinylacetylene. Hydrochloric acid is evolved during the reduction of palladium chloride and this causes an acidic reaction of the alcoholic solution with pH value being 1.4. Neutralization of the acid does not occur in hydrogenation of vinylacetylene in the presence of palladium precipitated on silica gel and the acidic reaction remained throughout the entire hydrogenation process. Hydrogenation of vinylacetylene in the presence of palladium precipitated on barium sulfate was run in a neutral medium. It was shown by analyses that the pH of the solution was not altered during the hydrogenation process. Hydrogenation of vinylacetylene with palladium catalyst in acidic or neutral medium did not differ in selectivity as shown by special experiments. In addition to this, we clarified the effect

of pH of the medium (over a wider range of its values) on the rate and the selectivity of hydrogenation. Various amounts of sodium hydroxide were added to the alcoholic solution obtained after the reduction of the catalyst until transitional values of pH from 1.4 to 14.0 were obtained. The experiments were run up to the degree of conversion of 35-45% at 0° with 300 rocking cycles of the apparatus per minute.

It is evident from the data in Table 4 that the rate increased notably and the reaction selectivity deteriorated at the same time with transition from an acidic medium to the alkaline medium. While the degree of hydrogenation of 30-35% was reached in 30 minutes in an acidic medium, the degree of hydrogenation of 40-45% was reached in but 15-20 minutes in an alkaline medium. Here, in the acidic medium at 34% degree of hydrogenation, no butylenes were detected, while in an alkaline medium, under the same conditions, the concentration of butylenes reached 10-12% with butadiene content of about 20%. Similar results in an alkaline medium were obtained also with palladium without a support and with palladium precipitated on barium sulfate.

The effect of the pH of the medium on the rate and the selectivity of hydrogenation of vinylacetylene may be explained by a decrease of selectivity of adsorption of vinylacetylene molecules in comparison with those of butadiene on the catalyst surface under the influence of hydroxide ions or by alteration of the character of intermediate compounds formed on the catalyst surface.

Hydrogenation of vinylacetylene in the presence of substances which retard the reaction. Data on hydrogenation of vinylacetylene in the presence of some inhibiting substances (mercury and copper acetates, hydrogen sulfide) are given in Table 5. These substances were introduced into the catalyst suspension in the form of dilute aqueous solutions after the reduction of the catalyst. All the substances worsened the selectivity of hydrogenation of vinylacetylene, even if present in insignificant amounts, and greatly retarded the reaction rate.

SUMMARY

1. The effect of the nature of the support and the solvent, the reaction temperature, the intensity of stirring of the solution and the pH of the medium were studied in connection with the rate and the selectivity of the reaction of hydrogenation of vinylacetylene in the presence of a palladium catalyst.

2. The intensity of stirring of the solution and the pH of the medium provided noticeable effect on the selectivity of the reaction, among all the other factors studied. The reaction proceeded unselectively at low stirring intensity. The reaction proceeded with a greater rate with lesser selectivity in alcoholic solution at pH value of over 7 than it did in acidic and neutral media.

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CATALYTIC HYDROGENATION OF VINYLACETYLENE FOR PREPARATION OF BUTADIENE

III. HYDROGENATION OF VINYLACETYLENE BY A CONTINUOUS METHOD

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In the previous papers [1] we have shown the possibility of selective hydrogenation of vinylacetylene in the presence of a palladium catalyst to the degree of 30-35% calculated on the acetylenic bond with 90-95% yield of butadiene calculated on the reacted vinylacetylene. The fundamental kinetic rules of selective hydrogenation of vinylacetylene in solution and the effect of various factors on the rate and the selectivity of the reaction were studied.

We made a study of hydrogenation of vinylacetylene in solution by a continuous method, with the aim of development of a technological process of hydrogenation of vinylacetylene and also for the check of the possible duration of workability of the catalyst without regeneration.

Vinylacetylene and hydrogen were passed in gaseous state through an alcoholic solution or that of some other solvent in which palladium on its support was present in a suspended state, with intensive stirring. The degree of hydrogenation of vinylacetylene with a continuous running of the process was determined by the proportion of hydrogen and vinylacetylene and also by the feed rate of the gaseous mixture. Under the condition of uniform distribution of vinylacetylene and hydrogen (intensive stirring) and with a definite proportion of hydrogen and vinylacetylene and with a definite rate of passage of the gaseous mixture, the reaction products consisted practically of butadiene (up to 30%) and unreacted vinylacetylene only (hydrogen being disregarded). A prolonged testing of the catalyst was run under the laboratory conditions for declining activity. The catalyst failed to lose its activity after 90 hours of continuous hydrogenation.

The laboratory data on the continuous hydrogenation of vinylacetylene were checked in a model installation with an iron apparatus with 2-liter capacity, provided with a stirrer. At 1:1 ratio of hydrogen and vinylacetylene and the feed rate of the gaseous mixture of 20 liters per hour per liter of solution, containing 0.6 g of palladium on 240 g of silica gel, the reaction products consisted of 22-25% butadiene, 1-2% butylenes and 75-78% unreacted vinylacetylene (hydrogen being disregarded). The possibility of continuous operation of the catalyst for 200 hours without a noticeable drop of activity or selectivity was shown.

Commercial hydrogen, obtained by the iron-steam method, turned out to be unsuitable for hydrogenation of vinylacetylene. The insignificant amounts of admixtures of carbon monoxide and sulfur compounds present in it completely poison the palladium catalyst. It was shown by our experiments that commercial hydrogen may be used for hydrogenation of vinylacetylene only after its having been purified over a catalyst consisting of nickel, chromium and copper deposited on silica gel.

We also checked the effect of impurities contained in vinylacetylene on the process of its hydrogenation and found that vinyl chloride, acetaldehyde and divinylacetylene (formed as by-products during dimerization of acetylene) do not exert a noticeable action on the rate and the selectivity of the hydrogenation reaction if they are added to vinylacetylene in an amount of 0.3-3.5%.

A method of regeneration of the worked-out catalyst was developed by the way of dissolution of palladium

in a mixture of hydrochloric and nitric acids with their subsequent removal by evaporation. In running the continuous experiments under laboratory conditions and with a model installation we showed that the hydrogenation proceeds with a regenerated catalyst at the same rate and selectivity as with the use of a freshly prepared catalyst.

EXPERIMENTAL

1) Hydrogenation of vinylacetylene in apparatus with porous glass filter. The apparatus consisted of a glass tube with 22-mm diameter and 150-mm length. A porous glass filter No. 2 was sealed into the lower end of the tube. A gaseous mixture of vinylacetylene and hydrogen was continuously bubbled through the catalyst suspended in the apparatus. The degree of hydrogenation was determined by the proportions of hydrogen and vinylacetylene and by the feed rate of the gas mixture. The degree of hydrogenation rose from about 15% to about 60% after a corresponding change of the hydrogen to vinylacetylene ratio from 1:2 to 2:1. For the same component proportion the degree of hydrogenation was decreased by increased feed rate of the gas mixture. The transition from periodic to continuous method of running the process did not exert any noticeable effect on the previously established dependence of reaction product composition on the degree of hydrogenation. A material effect on reaction selectivity in this instance, as in the periodic (batch) process, is exerted by the intensity of stirring of the solution. Thus, in experiments run without shaking of the reaction vessel, the hydrogenation proceeded unselectively. Thus, for increased yield of butadiene it is necessary to insure an intense stirring and good distribution of the gaseous mixture in the reaction medium.

A prolonged experiment was run with hydrogenation of vinylacetylene by the continuous method in acetic-acid solution. For this experiment we took 0.08 g of palladium, 6.0 g of silica gel and 20 ml of 95% acetic acid. An analysis of the reaction gas was run for the determination of alteration of catalyst activity in the process of hydrogenation after definite time intervals and a material balance of reaction products was made. It is evident from the data in Table 1 that, with the hydrogen to vinylacetylene proportion of 1.3:1 and at the feed rate of the gas mixture of 13-16 liters per hour per liter of solution, the reaction products consisted of about 35% butadiene and about 65% vinylacetylene. Butylenes also form along with butadiene after an increase of the degree of hydrogenation and their amount rises with the increased degree of hydrogenation. The catalyst did not lose its activity after 90 hours of continuous operation.

TABLE 1

Hydrogenation of Vinylacetylene by Continuous Method in Acetic-Acid Solution

Duration of experiment		Ratio of H_2 to vinylacetylene	Feed rate of gas mixt. (liters per hr/liter of solution)	Degree of hydrogenation (in %)	Reaction product composition (in volume %)		
of individual sample	from beginning of experiment				vinylacetylene	butadiene	butylenes
13 hr 30 min	13 hr 30 min	1.6 : 1	13.3	84.0	31.4	53.2	15.4
13 hr 35 min	27 hr 05 min	1.4 : 1	14.0	59.4	46.8	47.0	6.2
13 hr 15 min	40 hr 20 min	1.4 : 1	16.5	48.9	55.7	39.7	4.6
13 hr 00 min	53 hr 20 min	1.3 : 1	16.3	36.4	63.7	36.4	None
13 hr 45 min	67 hr 05 min	1.3 : 1	12.6	39.5	60.5	39.5	None
13 hr 30 min	80 hr 35 min	1.3 : 1	13.3	48.2	55.2	41.4	3.4
9 hr 30 min	90 hr 05 min	1.5 : 1	15.5	75.8	36.7	50.8	12.5

2) Hydrogenation of vinylacetylene in apparatus with stirrer. The running of prolonged experiments of continuous hydrogenation of vinylacetylene in the apparatus with a porous glass filter presented considerable difficulties owing to the frequent plugging of the filter by the catalyst. In order to eliminate these defects we made use of an apparatus with a stirrer. The apparatus consisted of a round-bottomed flask of 75-ml capacity. A tube with a drawn-out capillary end, to be used for supply of the gas mixture, was sealed into the bottom of the flask. The gas mixture was led into the solution in the form of fine bubbles which were distributed by an intensive stirring with the agitator rotating at about 400 rpm. 0.004 g of palladium, precipitated on 6 g of silica gel suspended in 20 ml of 95% ethyl alcohol, was taken for the reaction. It is evident from the data in Table 2 that with hydrogen to vinylacetylene ratio of 1:1 and with the feed rate of the gas mixture of 32-35 liters per hour per liter of solution, the degree of hydrogenation was 28-31% and practically only butadiene was the reaction product.

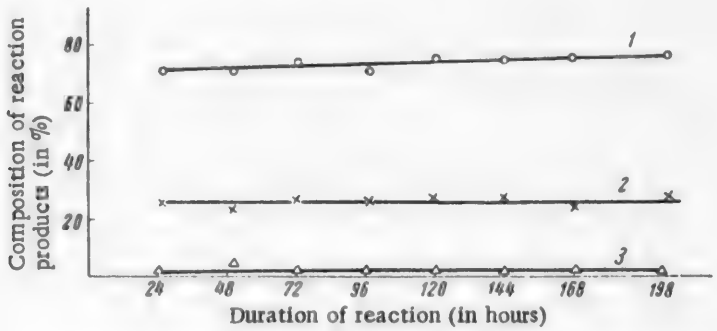
TABLE 2

Hydrogenation of Vinylacetylene by Continuous Method in Apparatus with a Stirrer

Ratio of H_2 to vinylacetylene	Feed rate of gas mixt. (liters per hr/liter of solution)	Degree of hydrogenation (%)	Composition of reaction products* (volume %)	
			vinylacetylene	butadiene
1.1 : 1	32	27.9	72.1	27.9
1.1 : 1	32	31.4	68.6	31.4
1 : 1	35	28.2	71.8	28.2
1 : 1	34	30.6	69.4	30.6
1 : 1	33	31.1	68.9	31.1

*No butylenes were present.

3) Hydrogenation of vinylacetylene in a model apparatus was run in an iron apparatus with 2-liter capacity. The stirring of the suspended catalyst was done by a stirrer rotating at about 350 rpm. The gas mixture entered the solution through a bubbler consisting of a ring-shaped tube with 1-mm openings. 1.3 g of palladium, precipitated on 240 g of silica gel, suspended in alcohol, was taken per charge. The total volume of the solution was 1300 ml. The reaction was run at 6-8°. Commercial vinylacetylene distillate and commercial, purified hydrogen were fed into the apparatus. The feed rate of hydrogen and vinylacetylene was controlled by rheometers. Part of the reaction products was condensed periodically and analyzed for the content of vinylacetylene, butadiene and butylenes. At hydrogen to vinylacetylene ratio of 1:1 and the feed rate of the gas mixture of 18-20 liters per hour per liter of solution, the reaction products consisted of 73-75% of vinylacetylene, 23-25% of butadiene and 1.5-3% of butylenes. These data are shown in the figure. The catalyst did not lose its activity and selectivity after some 200 hours of continuous operation.



Composition of reaction products depending on duration of operation of the catalyst: 1) vinylacetylene; 2) butadiene; 3) butylenes.

In order to raise the productivity of the process, we ran some experiments on hydrogenation of vinylacetylene in the same apparatus under pressure of 3 atmos at 40°. The amount of palladium and the total solution volume were the same as in experiments under normal pressure. The feed rate of hydrogen was regulated by a rotameter. Vinylacetylene entered the reactor from an evaporator and its amount was controlled by the rate of hydrogen feed and by the evaporator temperature. The ratio of hydrogen to vinylacetylene was 1:1 and the feed rate of the gas mixture was 200-120 liters per hour per liter of catalyst. It is evident from the data in Table 3 that with the degree of hydrogenation of 23-29% the reaction products contained 20-25% of butadiene and 1.5-3% of butylenes. Thus, the temperature rise to 40° and pressure rise to 3 atmos increased the productivity of the process

TABLE 3

Hydrogenation of Vinylacetylene in a Model Apparatus Under 3 atmos Pressure at 40°

Duration of hydrogenation of each sample (in hours)	Ratio of hydrogen to vinylacetylene	Feed rate of gas mixture (liters per hr/liter of solution)	Degree of hydrogenation (in %)	Composition of reaction products (in volume %)		
				vinylacetylene	butadiene	butylenes
6	1 : 1	100	36.6	66.0	34.0	1.3
6	1 : 1	100	63.4	46.0	44.6	9.4
6	1 : 1	100	62.5	45.4	46.5	8.0
7	1.1 : 1	120	69.2	42.0	46.8	11.2
6	1.1 : 1	120	52.3	54.8	38.1	7.1
6	1.1 : 1	100	64.5	44.9	45.7	9.4
8	1 : 1	110	60.6	47.4	44.6	8.0
6	1 : 1	100	29.2	72.6	24.9	2.5
6	1 : 1	100	29.2	73.4	23.3	3.3
6	1 : 1	120	26.6	74.9	23.6	1.5
6	1 : 1	100	29.4	73.1	24.4	2.5
6	1 : 1	100	23.3	78.1	20.5	1.4

Note: The variations of the degree of hydrogenation are mainly connected with alteration of the ratio of hydrogen to vinylacetylene.

of hydrogenation of vinylacetylene by 5-6-fold in comparison with the process of the reaction at normal pressure and 6-8° (with 15-20 liters per hour per liter of catalyst and up to 100-120). Some drop in selectivity is possibly connected with the insufficient intensity of stirring of the catalyst suspension under such conditions.

It was shown that formation of vinylacetylene polymers occurs under the conditions of running the hydrogenation reaction at elevated temperature. The amount of polymers formed in running the reaction at 40° was about 3% based on the amount of vinylacetylene introduced.

Regeneration of worked-out catalyst was done by two methods: 1) solution of palladium in a mixture of nitric and hydrochloric acids and their subsequent evaporation, and 2) solution of palladium in hydrochloric acid in the presence of chlorine. The regeneration was run as follows in the first method. The solvent was decanted from the catalyst and the latter was treated with small portions of a mixture of strong nitric and hydrochloric acids with heating on a steam bath. Palladium was thereby changed into palladium chloride and the tars present on the catalyst, as a result of polymerization of vinylacetylene, were oxidized. The palladium-chloride solution was decanted from the silica gel and evaporated to dryness, while the silica gel was washed with water and dried in a thermostat at 110°.

Experiments of hydrogenation of vinylacetylene with the regenerated catalyst were run both in the laboratory and in the model installation under normal pressure. It is possible to draw the conclusion, after a comparison of these data with those secured with the pure catalyst, that the composition of the reaction products remained the same. The activity of the regenerated catalyst failed to change in 100 hours of continuous operation.

The regeneration of the catalyst by the second method was done as follows. The alcohol was decanted from the catalyst and the latter was washed with acetone to remove the tars. Hydrochloric acid was poured into the catalyst and chlorine was passed into it, whereupon palladium was transformed into palladium chloride. The reduction of palladium chloride to palladium by means of molecular hydrogen was done in the same hydrochloric-acid solution, the palladium precipitating on the same silica gel. The hydrochloric acid was decanted and was used for the regeneration of the next batch of the catalyst, while the palladium on silica gel was washed with water until neutral. The results of the laboratory experiments run with this catalyst did not differ from the data obtained with the catalyst regenerated by the first method.

SUMMARY

1. The process of hydrogenation of vinylacetylene may be realized by a continuous process under the conditions of intensive stirring of the solution and uniform gas distribution. It was shown that, in this case, the catalyst preserves its activity for over 200 hours.

2. The possibility of regeneration of the spent catalyst with its use for hydrogenation of vinylacetylene without a drop in activity or selectivity of the process was demonstrated.

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BROMINATION OF UNSATURATED COMPOUNDS

VII. KINETICS AND MECHANISM OF ADDITION OF BROMINE TO THE DOUBLE BOND IN THE PRESENCE OF BROMIDES

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The study of the kinetics of the reaction of addition of bromine to a double bond in aqueous solution is complicated by the fact that two products are formed in this reaction – the bromohydrin and the dibromo derivative. The formation of the bromohydrin is accompanied by the evolution of hydrogen bromide which then takes part in the course of the process by altering the reaction rate and the quantitative ratio of its two products indicated above.

It is known from the literature data that hydrogen bromide is a strong catalyst in reactions with unsaturated compounds which proceed in chloroform and carbon tetrachloride solution [1]. In most cases the hydrogen bromide and bromides accelerate the addition of bromine to the double bond in acetic-acid solution [2]. Conversely, a retardation of the reaction is observed in methanol [3] or aqueous solution [4]. The mechanism of action of bromides has been also much discussed in the literature. Anantakrishnan and Venkataraman [5] proposed the chain mechanism including the complex A·HBr and bromine activated by the same acid. Nozaki and Ogg [6] concluded that the reactions catalyzed by bromides proceed, in glacial acetic acid, as trimolecular processes of interaction of the unsaturated compound with bromine and bromide ion with the unsaturated compound. Robertson and his co-workers, who have studied the addition of bromine also in acetic acid, consider that HBr forms with bromine a complex compound HBr_3 which may be an electrophilic reagent in reactions with some unsaturated compounds and a nucleophilic one with other unsaturated compounds [7]. Bartlett and Tarbell [3] ascribed a weak, electrophilic action to the complex Br_3^- in comparison with the more active bromine molecules.

In the present paper we present some results of a study of the reaction of addition of bromine in the presence of a bromide in aqueous solution.

EXPERIMENTAL

It has been established previously, in the study of the effect of the bromide ion on the kinetics of the addition reaction, that the reaction rate may be represented by the following kinetic equation which has a general significance for the compounds shown in the paper [8, 3].

$$-\frac{d(Br_2)}{dt} = k'[A]\,[Br_2] + k''[A]\,[Br_3^-], \qquad (1)$$

where $[Br_2]$ is the analytical concentration of active bromine and [A] is the concentration of the unsaturated compound. By determining the values of the rate constants k' and k" for various unsaturated compounds, we discovered that the ratio k'/k" depends on the electron density in the region of the double bond. This dependence is shown in Table 1 from the data in which it is evident that k' is considerably greater than k" for compounds placed at the beginning of the table. The reduction of the rate constant k' of the reaction with bromine for the following compounds is accompanied by the decrease of rate constant k" for the reaction with Br_3^-, as well. But, since the reduction of k" proceeds to a lesser degree than that of k', the value of k" becomes greater than that of k' for the last two compounds. Thus, along with the reduction of the reactivity of the double bond, the fraction of the substance reacting with Br_3^- increases constantly.

TABLE 1

Dependence of k'/k" on the Reactivity of the Unsaturated Compound

Unsaturated compound	Rate constants for the reaction (liters/mole·min) with Br_3^- (k')	with Br_3^- (k'')	$\frac{k'}{k''}$
$CH_3CH{=}CHCOOH$ (I)	3000	22	130
$C_6H_5CH{=}CHC_6H_5$ (II)	200	2.02	99
$^-SO_3CH_2CH{=}CHCH_2SO_3^-$ (III)	23	0.47	49
$^-O_2CCH{=}CHCO_2^-$ (IV)	16.7	1.65	10
$[(CH_3)_3NCH_2CH{=}CH_2]^+$ (V)	2.03	0.6	3.4
$^-HO_2CCH{=}CHCO_2H$ (VI)	0.033	0.023	1.5
$CH_3O_2CCH{=}CHCO_2^-$ (VII)	0.0090	0.018	0.5
$[(CH_3)_3NCH{=}CH_2]^+$ (VIII)	0.00010	0.00040	0.25

It appeared later that the proportion of the reaction products, specifically of bromohydrin and dibromide, depends not only on the bromide ion concentration as supposed by Bartlett and Tarbell [3], but also on the reactivity of the unsaturated compound: the smaller is the latter, the more dibromide is formed, as this is evident from the data in Table 2.

The cited experimental material permits us to suppose that the dibromide is formed as a result of action of the tribromide ion on the unsaturated compound or as a result of combined action of bromine and the bromide ion. These two possibilities are indistinguishable kinetically since:

$$[Br_3^-] = \frac{1}{K}[Br_2][Br^-].$$

For a confirmation of this supposition, we studied in more detail the effect of the bromide ion on the formation of dibromide for compound (V). The results of this study are shown in the figure in which the concentrations of sodium bromide from 0 to 1 mole/liter are plotted on the abscissa axis, while the percent of resulting dibromide of (V) are plotted on the ordinate axis. The resulting curve 1 shows the mutual dependence of these values at 0°. Curve 2, located in the same figure, shows the change of Br_3^- concentration along with the change of NaBr concentration, while the Br_3^- concentration is shown in percent of active bromine (the bromine concentration was the same for all experiments). Both curves have the same form which may indicate the close tie between the values shown by these curves.

TABLE 2

Dependence of Dibromide Formation on Reactivity of C–C

Unsaturated compound	k' of react. with Br (liter/mole·min)	Salt	Salt conc. (moles/liter)	% of dibromide
(I)	3000	KNO_3	0.10	0
		NaBr	0.05	5
		NaBr	0.20	11
(II)	200	KBr	0.10	10
		KBr	0.20	17
(V)	2.03	KNO_3	0.1	6
		NaBr	0.05	24
		NaBr	0.20	56
		KCl	0.20	17
(VII)	0.0090	KNO_3	0.1	2
		NaBr	0.05	59
		NaBr	0.20	84
		KCl	0.20	50
(VIII)	0.00010	$NaNO_3$	0.20	0
		NaBr	0.24	92

TABLE 3

Direction of Reaction of (V) with Bromine at Various Levels of Br^-

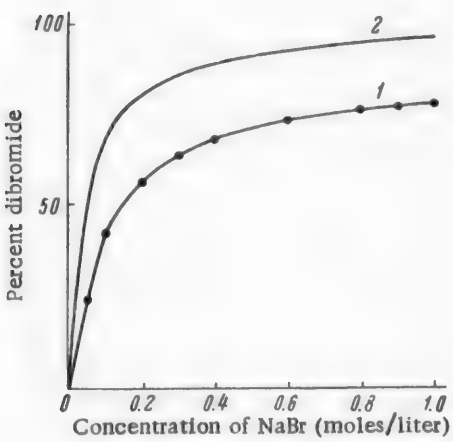
Temperature	20°	20°	12°	20°
[NaBr]	0.05	0.100	0.200	0.800
Reaction proceeds through Br_3^- by:	25%	38%	55%	70%
Amount of dibromide (in %)	25	42	57	73

In addition, we ran some kinetic experiments with determination of the amount of dibromide after termination of the reaction at 20° and 12°. As indicated above, the reaction rate is expressed by Eq. (1). Since the rate constants k' and k" in this equation are known, having determined the reaction rate, one may determine by a calculation what fraction of (V) is transformed via the first and what fraction via the second route of the reaction, i.e., via Br_2 or via Br_3^- (or $(1/K)[Br_2][Br^-]$).

The results shown in Table 3 indicate that, in reality, the first member of the kinetic equation approximately reflects the rate of bromohydrin formation, while the second member shows the rate of dibromide formation. This conclusion follows from the fact that at different bromide concentrations the percent of the reaction rate with Br_3^-, relative to the total rate of bromination, is approximately equal to the percent content of dibromide in the product.

DISCUSSION OF RESULTS

The conception of the reaction mechanism in the presence of the bromide meets some difficulties. If one considers that, in this case, two electrophilic agents Br_2 and Br_3^- [3] are operative, one should think that the electrophilic character of bromine should be always stronger than that of Br_3^-. However, it follows from the data in Table 1 that, conversely, Br_3^- is more active than Br_2 in the reaction with compounds (VII) and (VIII).



Dependence between percent of dibromide formation from (V) and the concentration of NaBr. Explanation in the text.

The supposition that Br_3^- may be an electrophilic and nucleophilic reagent [7] evidently agrees with the data in Table 1: the weakly electrophilic Br_3^- gradually changes into the nucleophilic reagent. However, the bromide ion present in the solution should be a stronger nucleophilic agent than Br_3^- and, if the double bond acquires an electrophilic character under the influence of the electron-acceptor groups present in the molecule of the unsaturated compound, Br^- should react first and not Br_3^-. For this reason, this mechanism also seems doubtful.

It is possible, finally, to consider that Br_3^- is an extremely weak electrophilic agent and for this reason its brominating action for our compounds may be disregarded while the double bond is always effectively attacked only by a bromine molecule. Depending on whether water or the bromide ion is the third partner in the reaction of bromine with the unsaturated compounds, the process proceeds along two paths. The first of these paths leads to the bromohydrin formation, the second — to dibromide. The solvent (water) does not enter the kinetic equation since its concentration remains constant. In this case, the rate-determining step of the process would be the stage of formation of the transition complex of three particles — unsaturated compound, bromine and water, or bromide ion.

It remains beyond understanding, with such a concept, in what manner does the reactivity of the unsaturated

compound, as shown in Table 1, have any significance in the competition of water with the bromide ion for the participation in the reaction. An explanation of this phenomenon may be found in the assumption that the bromide ion, in the case of low electron density at one of the unsaturated carbons owing to the electrostatic attraction, forms a complex compound with the unsaturated molecule. Formation of complexes of unsaturated compounds with hydrogen bromide has been noted in the literature and these are regarded as a state of a preliminary activation of the molecules prior to the addition of hydrogen bromide or bromine [9, 5]. Hydrogen bromide also accelerates the transformation of maleic acid into fumaric [10]. Such a complex with HBr or Br^- should possess a greater electron-donor ability and should enter more readily into a compound with bromine, forming the dibromide invariably thereby. It is possible to suppose that this reaction mechanism belongs to the addition of bromine to unsaturated compounds with low electron density in the region of the double bond. For compounds which readily react with bromine another mechanism is probable which includes into the reaction the weakly electrophilic reagent Br_3^-. The form of the kinetic equation is not changed thereby.

SUMMARY

1. The bromohydrin is a reaction product in the action of bromine water on an unsaturated compound. The dibromo derivative is formed in the presence of the bromide ion with its participation.

2. The role of the bromide ion as a reaction participant increases with decreased reactivity of the double bond.

3. The proportion of the amounts of bromohydrin and dibromide in the reaction products depends not only on the concentration of the bromide ion in solution, but also on the reactivity of the unsaturated compound: the lower is the latter, the more dibromide is formed.

4. A discussion of the possible reaction mechanisms is presented.

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CONCERNING THE CHARACTERIZATION OF α,β-UNSATURATED KETONES. VII.

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One of us cited in the preceding paper [1] some data which prove the dependence of the ability toward hydrolytic cleavage of structurally different aliphatic α,β-unsaturated ketones and the degree of conjugation of >C=C< and C=O bonds in them. The alkaromatic α,β-unsaturated ketones have not been studied in this connection. At the same time, an all-sided study of this problem is important from the viewpoint of clarification of the mechanism of the transfer of atomic effects.

The present work is the first publication of experimental data on the hydrolytic cleavage of alkaromatic α,β-unsaturated ketones which contain an aryl radical directly bound to the carbonyl group. Ketones of this type have been prepared by the way of dehydration of β-ketols synthesized by the Grignard-Colonge method [2].

$$(CH_3)_3C-\underset{}{\overset{CH_3}{\overset{|}{C}}}=O + CH_3COAr \xrightarrow{C_6H_5N(CH_3)MgI} (CH_3)_3C-\underset{OH}{\overset{CH}{\overset{|}{\underset{|}{C}}}}-CH_2COAr$$

Experiments on hydrolytic cleavage of β-ketols were also run by us. The data in Table 2 indicate that β-ketols are considerably more labile than the α,β-unsaturated ketones corresponding to them and are more sensitive to very weak hydrolytic agents. In addition, the behavior of β-ketols in hydrolysis differs from that of the α,β-unsaturated ketones in that the alteration of concentration of sodium hydroxide exerts only a feeble influence on the degree of cleavage of β-ketols, while it influences rather strongly the hydrolytic cleavage of α,β-unsaturated ketones on the other hand. The rate of hydrolysis of alkaromatic ketones studied by us is considerably decreased by increased concentration of sodium hydroxide from 0.01 to 0.1 N. In this respect, these ketones somewhat resemble mesityl oxide and 3-methyl-3-hepten-5-one which are cleaved more completely in the presence of 0.1 N sodium hydroxide solution.

It should be noted also that, of the four homologous β-ketols, the most stable was the β-ketol (I) with phenyl radical and only from this ketol was there obtained, on distillation under 3-mm vacuum with trace of iodine, the corresponding α,β-unsaturated ketone in 81.7% yield, while the homologs of this ketol underwent mainly a thermal decomposition during such treatment.

EXPERIMENTAL

1. The syntheses of β-ketols were run in a four-necked flask, the central neck of which was fitted with a mechanical stirrer, while the side necks were provided with a thermometer, a dropping funnel and a bulb reflux condenser whose open end could be connected to a gasometer through a system of two U-tubes with calcium chloride. Methylmagnesium iodide was prepared for all experiments from 0.25 g-atoms of magnesium, 0.29 mole of methyl iodide and 150 ml of absolute ether. To the solution we carefully added, with external ice cooling, an ethereal solution (1:1) of 0.25 mole of thoroughly dried methylaniline. The yield of methylanilinomagnesium iodide was estimated by the amount of methane formed; this yield varied within the range of 94-98%. The amounts of pinacolone and CH_3COAr, where Ar = C_6H_5, $C_6H_4CH_3$-p, $C_6H_4C_2H_5$-p and $C_6H_4CH(CH_3)_2$-p, needed

for running the β-ketol syntheses, were adjusted according to the yield of the latter substance. Pinacolone in 1:1 solution in absolute ether was added over 20 minutes. After a 30-minute hold, an absolute ether solution (1:1) of the methylaryl ketone was added over one minute. The reaction mixture was stirred for one hour longer and then was decomposed, with external ice cooling, with 50 ml of ice water. Extraction of methylaniline from the reaction products was done by their being repeatedly treated with 5% hydrochloric acid solution; then, the ethereal solution was washed with a dilute sodium carbonate solution, water, and was dried over anhydrous sodium sulfate. The residues crystallized after filtration of the sodium sulfate and distillation of the ether. The purification of the β-ketols was done by crystallization from petroleum ether with b.p. up to 55°.

a) 2,3,3-Trimethyl-5-phenyl-3-pentanol-5-one (I). The yield of the β-ketol, if the methylaniline and the ketones were introduced into the reaction in absolute benzene solution, was but 12-15%, while in the medium of absolute ether it was 47.5%. M.p. 74.5°.

Found %: C 76.02; H 8.93; OH 8.07. M 216.2 (by Rast method). $C_{14}H_{19}O(OH)$. Calculated %: C 76.32; H 9.15; OH 7.72. M 220.3.

b) 2,3,3-Trimethyl-5-p-tolyl-3-pentanol-5-one (II). Obtained in 30.5% yield; m.p. 80.5°.

Found %: OH 7.03. M 226.3 (cryoscopically). $C_{15}H_{21}O(OH)$. Calculated %: OH 7.26. M 234.33.

c) 2,2,3-Trimethyl-5-p-ethylphenyl-3-pentanol-5-one (III). The yield of the β-ketol was 32.5%; m.p. 65°.

Found %: OH 6.87. M 245.6 (by Rast method). $C_{16}H_{23}O(OH)$. Calculated %: OH 6.85. M 248.35.

d) 2,2,3-Trimethyl-5-p-isopropylphenyl-3-pentanol-5-one (IV) was obtained in 20.5% yield; m.p. 79°.

Found %: OH 6.46. M 260.7 (by Rast method). $C_{17}H_{25}O(OH)$. Calculated %: OH 6.48. M 262.38.

2. Transformation of β-ketols into the corresponding α,β-unsaturated ketones. a) β-Ketol (I) after distillation with traces of iodine under 3 mm gave an 81.7% yield of 2,2,3-trimethyl-5-phenyl-3-penten-5-one (V),– a liquid with b.p. 122° at 3 mm.

d^{20}_4 0.9586, $n^{20}D$ 1.5350, MR_D 65.69, M 199.0. $C_{14}H_{18}OF_4$. Calculated: MR_D 62.74, M 202.28. Data on bromination are given in Table 1.

b) β-Ketol (II) gave, on distillation with traces of iodine at 3 mm, only a 12.5% yield of 2,2,3-trimethyl-5-p-tolyl-3-penten-5-one (VI). Hence, the dehydration of this β-ketol, as well as of β-ketols (III), and (IV), was run by heating the solution of the β-ketol in ethylene chloride (1 g ketol per 4 ml of ethylene chloride) with a few crystals of iodine for 4-8 hours on a steam bath. The yield of ketone (VI) in this case was 42%. It is a liquid with b.p. 131-132° at 2 mm.

d^{20}_4 0.9570, $n^{20}D$ 1.5340, MR_D 70.26, M 218.2 (by Rast method). $C_{15}H_{20}OF_4$. Calculated: MR_D 67.37, M 216.31. Data on bromination are given in Table 1.

c) β-Ketol (III) was transformed into 2,2,3-trimethyl-5-p-ethylphenyl-3-penten-5-one (VII) in 81.5% yield; it is a liquid with b.p. 137° at 2.5 mm.

d^{20}_4 0.9519, $n^{20}D$ 1.5335, MR_D 75.16, M 235.4 (by Rast method). $C_{16}H_{22}OF_4$. Calculated: MR_D 72.03, M 230.34. Data on bromination are given in Table 1.

d) β-Ketol (IV) was transformed into 2,2,3-trimethyl-p-isopropylphenyl-3-penten-5-one (VIII) in 45% yield; it is a liquid with b.p. 142-143° at 1.5 mm.

d^{20}_4 0.9462, $n^{20}D$ 1.5280, MR_D 79.53, M 240.8 (by Rast method). $C_{17}H_{24}OF_4$. Calculated: MR_D 76.65, M 244.38.

The resulting ketones showed rather high values of exaltations: (V) +2.95, (VI) +2.89, (VII) +3.13 and (VIII) +2.88, which evidently is caused by the creation of a crossed system of double bonds through the π-electrons of the benzene nucleus. According to data [3], phorone shows an exaltation of +2.38.

Despite the presence of a quaternary carbon atom at the ethylenic bond in these ketones, they yield rather stable dibromides, which fact is connected with the stabilizing influence of aryl radicals present in them [4].

3. A study of hydrolytic cleavage of α,β-unsaturated ketones and β-ketols. Samples of these substances

TABLE 1

Ketones	Sample (in g)	Amt of Br sol. in CCl_4 (in ml)	Amt of 0.1 N $Na_2S_2O_3$ solution (ml)			Iodine number (theoretical)	Found values of iodine numbers			Passage of bromine into HBr, relative to total bromine consumption (in %)
			used for titration of excess halogen	corresponding to halogen consumption	used for iodine from HI		total	from cleavage	from addition	
(V) .	0.0788	5	13.75	7.60	0.20	125.49	122.42	6.44	115.98	2.63
(VI) . .	0.1080	5	11.02	10.33	0.04	117.36	121.39	0.94	120.45	0.38
(VI) . .	0.1043	5	12.18	9.17	0.29	110.18	111.49	7.11	104.38	3.16

of about 0.0025 mole were dissolved in 5 ml of anhydrous methanol and, after addition of 10 ml of 0.01-N sodium hydroxide solution (Table 2, expt 1) or 10 ml of 0.1-N sodium hydroxide solution (Table 2, expt 2), were heated in sealed ampoules for two hours on a steam bath. The ampoule contents, after being cooled, were quantitatively transferred into a flask with 50 ml of 0.1-N iodine solution. Then 25 ml of 1-N sodium hydroxide solution was added and the mixture was allowed to stand for 15 minutes. After acidification with 26 ml of 1-N solution of hydrochloric acid, the excess iodine was back titrated with 0.1-N hyposulfite solution. The calculation of the degree of hydrolytic cleavage of the α,β-unsaturated ketones and β-ketols was related to the consumption of 6 moles of iodine per 1 mole of the substance (100% cleavage).

TABLE 2

Expt. No.	Substances used	Sample (g)	Volume 0.1 N $Na_2S_2O_3$ solution (in ml)*		Degree of hydrolytic cleavage (% of theoretical)
			for titration of excess iodine	for iodine consumed	
1	Ketone (V)	0.0534	49.68	0.22	0.69
2	Ketone (V)	0.0480	44.71	5.19	18.19
1	Ketone (VI)	0.0522	49.73	0.17	0.58
2	Ketone (VI)	0.0538	46.88	3.02	10.11
1	β-Ketone (I)	0.0556	24.00	25.90	86.30
2	β-Ketone (I)	0.0532	23.70	26.20	91.22
1	β-Ketone (II)	0.0570	25.92	23.98	82:15
2	β-Ketone (II)	0.0578	24.76	25.14	84.93
1	β-Ketone (III)	0.0621	22.81	27.09	90.26
2	β-Ketone (III)	0.0620	24.32	25.58	85.11
1	β-Ketone (IV)	0.0658	23.90	26.00	86.41
2	β-Ketone (IV)	0.0646	24.65	25.25	85.44

*The volume of 0.1-N $Na_2S_2O_3$ solution in all experiments that was consumed for titration in a blank experiment was equal to 49.9 ml.

SUMMARY

1. β-Ketols, synthesized for the first time, were described: 2,2,3-trimethyl-5-phenyl-3-pentanol-5-one, 2,2,3-trimethyl-5-p-tolyl-3-pentanol-5-one, 2,2,3-trimethyl-5-p-ethylphenyl-3-pentanol-5 one and 2,2,3-trimethyl-5-p-isopropylphenyl-3-pentanol-5-one, as were the corresponding α,β-unsaturated ketones: 2,2,3-trimethyl-5-phenyl-3-penten-5-one, 2,2,3-trimethyl-5-p-tolyl-3-penten-5-one, 2,2,3-trimethyl-5-p-ethylphenyl-3-penten-5-one and 2,2,3-trimethyl-5-p-isopropylphenyl-3-penten-5-one.

2. The degree of hydrolytic cleavage of these β-ketols and α,β-unsaturated ketones was determined and it was shown that the latter ketones are brominated with an insignificant loss of hydrogen bromide, which fact is a deviation from the M.D. L'vov-D.V. Tishchenko reaction.

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DEUTERIUM EXCHANGE BETWEEN LIQUID DBr AND PHENYLATED ALKANES

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The rate of reactions of electrophilic substitution of hydrogen in alkylbenzenes (chlorination [1, 2], bromination [3], nitration [4] and Friedel-Crafts alkylation [5]) decreases in the series: $C_6H_5CH_3 > C_6H_5C_2H_5 > C_6H_5CH(CH_3)_2 > C_6H_5C(CH_3)_3$. This is explained [6, 7] by the hyperconjugation effect (σ,π-conjugation). By analogy it is possible to suppose that the rate of the corresponding reactions of polyphenylated alkanes also depends on the proportion between the number of α-CH bonds and the number of the aromatic rings. If one considers that the rate of bromination of alkylbenzenes depends on the branching of the hydrocarbon chain not only at the α- but also at the β-carbon atom of the alkyl group [3], then it is not impossible that proportion between the number of the rings and the number of more removed CH-bonds may have a significance in the reactions electrophilic substitution of hydrogen in other phenylated alkanes.

In order to verify the correctness of these suppositions, we turned to the study of deuterium exchange between polyphenylated alkanes and liquid deuterium bromide [8, 9]. Its mechanism is close to that of chemical reactions of electrophilic substitution of hydrogen [10].

Some preliminary results have been published previously [11].

EXPERIMENTAL

Compounds. Diphenylmethane. 1) Kahlbaum product. Vacuum distilled. 2) Product of Kharkov Reagent Plant. Vacuum distilled. 3) Same product, frozen out twice. M.p. 26.5° (26°).•

Triphenylmethane. 1) Eastman Kodak product. Recrystallized from alcohol, vacuum sublimed. M.p. 91.1-91.8°. 2) Same product, recrystallized twice from alcohol. M.p. 92.2-92.5°.

Tetraphenylmethane. Synthesized in benzene solution from triphenylmethyl chloride and ether-free phenylmagnesium bromide [12]. Yield: 17%. Three times recrystallized from benzene. M.p. 282.5-283.5° (284°).

Fluorene. 1) Eastman Kodak product. Vacuum distilled. M.p. 115° (113°). 2) Additionally recrystallized.

Dibenzyl. 1) Domestic product. Vacuum distilled. 2) Eastman Kodak product. Vacuum distilled. 3) Domestic product, triply distilled. M.p. 51-52° (51-52°).

Diphenylethane. Synthesized from 1,1-diphenylethylene by reduction using Clemmensen method [13]. Yield: 37%. Vacuum distilled. B.p. 135-136° (12 mm), 268-270° (760 mm), $n^{20}D$ 1.5760 (1.5762).

sym-Tetraphenylethane. Diphenylbromomethane was prepared from diphenylmethane (yield 56%) [14] and tetraphenylethane was synthesized (yield: 44%) from the latter by condensation in the presence of granulated zinc in dry ethyl acetate. Recrystallized four times from a mixture of alcohol and benzene (1:2). M.p. 211-212° (211-212°).

•In parentheses, both here and further, we indicate the constants of the substance after the performance of the kinetic experiment.

1,1,1-Triphenylethane. Prepared [15] by the Grignard reaction from triphenylbromomethane and methyl iodide (yield: 66%). Recrystallized three times from alcohol. M.p. 94.2-94.7° (93.2-93.7°).

1,3-Diphenylpropane. Calcium phenylacetate was subjected to dry distillation [16]. The dibenzyl ketone (obtained in 90% yield) was reduced by the Kizhner method [17], which was modified in some details. This method was better both as to yield (61%) and the purity of the product, than the Clemmensen method [18].

Found %: C 92.14; H 8.14. Calculated %: C 91.78; H 8.22. B.p. 155-156° (9-10 mm), 302° (760 mm), d^{20}_{20} 0.9820, $n^{20}D$ 1.5560 (1.557), MR_D 64.29; calculated 64.26.

1,4-Diphenylbutane. 1) Synthesized by G.S. Kolesnikov and kindly given to us. M.p. 52°. 2) The same product after additional recrystallization from a mixture of benzene and alcohol (1:9). M.p. 52.2-53.0° (52-52.5°).

1,5-Diphenylpentane. Synthesized similarly to diphenylpropane. Dibenzylacetone (90% yield) was obtained from calcium hydrocinnamate, and the diphenylpentane was prepared from the latter. After five redistillations at 165-170° (9 mm), the yield was 27%; d^{20}_{20} 0.9674, $n^{20}D$ 1.5492 (1.5492). MR_D 73.58, calculated 73.49.

Experimental technique. The technique was the same as in the previous work [19]. All substances were soluble in liquid hydrogen bromide,* and the solutions of some of the substances were colored (most often yellow); at times, the color intensity (and even the color itself of the solution) changed with time or after cooling of the solution. The substances were purified by redistillation after the experiment or by a sublimation, after which the constants were redetermined (m.p., index of refraction), and these confirmed the absence of chemical changes.

Experimental results. The experimental results are collected in Table 1, where t is the duration of the experiment in hours,** P_S/P_{sub} is the ratio of the weight of solvent to the weight of the substance, C^0_S and C_{sub} are the concentration of deuterium (in atom %) in the hydrogen bromide before the experiment and in the water from combustion of the substance after the run. For most substances, several series of experiments were run with different times, as is evident from values of C^0_S. The number of exchanged atoms n was calculated by the previously cited formula [20].***

It was assumed in the calculations that, under the experimental conditions, three hydrogen atoms (in ortho and para positions) are capable of exchange in each phenyl group.

DISCUSSION OF RESULTS

In Table 2 we indicate the average values of n for times of 1 and 6 hours, calculated for one phenyl group. The values of n for benzene, diphenyl and alkylbenzenes were taken from other publications [8, 9]. Since the hydrogen atoms of aliphatic CH-bonds in alkaromatic hydrocarbons do not exchange with deuterium bromide [9], the values of n for the same duration of experiments characterize the relative reactivity of the aromatic rings in phenylated alkanes.

Data for group I of the substances permit one to judge the dependence of the reactivity of the hydrocarbon on the type of bond conjugation. Thus, in the diphenyl molecule, the para and ortho hydrogen atoms exchange more rapidly than in the benzene molecule by three orders of magnitude: $k_{C_6H_6} = 5 \cdot 10^{-8}$; $k_{C_{12}H_{10}} = 7\text{-}2 \cdot 10^{-5}$. This is evidently a consequence of the conjugation of π-electrons of two aromatic rings (π,π-conjugation).

It is evident from the experimental results on isotopic exchange of hydrogen in tetraphenylmethane that the phenyl groups affect considerably their mutual reactivity even if they are separated by a carbon atom and the usual conjugation of π-electron systems of two aromatic rings (π,π-conjugation) is absent. The hydrogen in tetraphenylmethane is exchanged for deuterium at a rate that is greater by two orders of magnitude than in benzene. The spectroscopic data agree well with the conclusion concerning the transfer of the mutual effects of phenyl groups which are not directly connected to each other. For example, V.F. Lavrushin [21] has found that the intensity of medium ultraviolet absorption bands in the spectra of polyphenylmethanes greatly exceeds the value

*Only in two experiments with $(C_6H_5)_4C$ (24 and 96 hours) was there a small amount of an undissolved substance.

**The number of stars corresponds to the number of the preparation.

***Part of the hydrogen atoms of fluorene is apparently exchanged very rapidly, and this leads to the too high value of n owing to the increase of the deuterium distribution coefficient during the freezing of the solution for termination of the reaction [10].

TABLE 1

Results of Experiments on Deuterium Exchange with Liquid DBr

t	P_s/P_{sub}	C_s°	C_{sub}	n
		$(C_6H_5)_2CH_2$		
1*	47	5.41	0.40	0.4
1*	39	5.41	0.50	0.6
1***	24	12.8	0.92	0.5
1***	31	12.8	0.92	0.5
2*	54	1.81	0.26	0.8
2*	55	1.81	0.26	0.8
3.2*	87	1.37	0.37	1.4
6*	76	5.41	1.84	1.8
6**	75	5.41	1.84	1.8
6**	34	2.69	0.88	2.0
6**	36	2.69	0.86	1.9
6**	28	2.69	0.82	2.0
280*	41	1.37	1.79	7.5
1450*	51	1.37	2.12	8.4
		$(C_6H_5)_4C$		
1	131	5.36	0.20	0.3
1	119	5.36	0.21	0.3
6	124	6.44	1.06	1.4
6	125	6.44	1.05	1.4
6	110	6.44	0.98	1.3
24	78	12.8	3.6	2.9
96	58	12.8	3.65	2.8
		$C_6H_4CH_2C_6H_4$ – fluorene		
10 min **	42	5.36	5.71	5.1
10 min **	33	5.36	5.27	5.7
1**	40	5.36	5.71	5.1
1**	35	5.36	5.52	5.1
3*	54	1.37	1.96	6.2
6*	121	1.37	2.30	6.7
280*	86	1.37	3.66	10.8
		$(C_6H_5)_2CHCH_3$		
1	44	12.8	1.79	1.0
1	46	12.8	1.86	1.1
6	33	2.69	1.19	2.8
6	59	2.69	1.20	2.6
		$(C_6H_5)_3CCH_3$		
6	42	2.69	0.50	1.6
6	43	2.69	0.48	1.5
		$(C_5H_5)_2CHCH(C_6H_5)_2$		
1	36	12.8	1.16	1.0
1	37	12.8	1.28	1.3
6	46	2.69	1.18	4.2
		$C_6H_5(CH_2)_3C_6H_5$		
1	34	12.8	2.53	1.7
1	28	12.8	2.42	1.7
6	49	2.69	1.59	4.3
6	42	2.69	1.59	4.4
		$(C_6H_5)_3CH$		
1*	79	5.41	0.07	0.09
1*	66	5.41	0.07	0.09
1*	49	12.8	0.24	0.16
1*	36	12.8	0.19	0.13
1**	54	12.8	0.22	0.14
1**	43	12.8	0.29	0.19
3.2*	92	1.37	0.06	0.29
6*	83	1.37	0.11	0.54
6*	94	5.41	0.44	0.57
6*	95	5.41	0.44	0.57
280*	104	1.37	1.53	7.3
1450*	120	1.39	2.36	11.0
		$C_6H_5(CH_2)_2C_6H_5$		
1**	108	1.63	0.21	0.7
1**	65	5.41	0.61	0.7
1**	70	5.41	0.58	0.7
1***	33	12.8	1.38	0.8
1***	48	12.8	1.40	0.8
3.3*	90	1.37	0.46	1.9
6*	113	1.37	0.72	3.0
6**	95	1.63	0.77	2.7
6**	100	5.41	2.72	3.0
6**	114	5.41	2.72	3.0
6***	64	2.69	1.31	3.0
6***	64	2.69	1.29	2.9
12**	78	1.63	1.17	4.2
24**	95	1.63	1.55	5.5
22**	110	1.63	2.01	7.0
		$C_6H_5(CH_2)_4C_6H_5$		
1*	116	1.66	0.39	1.6
1*	110	5.41	1.31	1.8
1*	80	5.41	1.31	1.9
6*	78	1.63	0.90	4.4
6**	72	2.69	1.99	5.6
6**	57	2.69	1.98	5.8
12*	92	1.63	1.27	5.7
327*	100	1.63	1.66	7.4
		$C_6H_5(CH_2)_5C_6H_5$		
1	33	12.8	2.90	2.4
1	37	12.8	2.80	2.3
6	45	2.69	1.54	5.2
6	32	2.69	1.46	5.3

TABLE 2

Comparison of the Number of α- and β-CH-Bonds, per One Phenyl Group, with the Average Number of Exchanged Hydrogen Atoms n

Group	Formula	α-CH / C_6H_5	β-CH / C_6H_5	Exchanged number of atoms n	
				in 1 hr	in 6 hr
I	$(C_6H_5)_4C$			0.08	0.3
	C_6H_6			0.0001	—
	$C_6H_5C_6H_5$			0.65	1.7
	$C_6H_5CH_2C_6H_5$			0.25	0.9
	$C_6H_4CH_2C_6H_4$			2.6	3.4
II	$C_6H_5CH_3$	3	—	1.0	2.3
	$(C_6H_5)_2CH_2$	1	—	0.25	0.9
	$(C_6H_5)_3CH$	1/3	—	0.04	0.16
	$(C_6H_5)_4C$			0.08	0.3
III	$C_6H_5CH_2CH_3$	2	3	1.0	2.4
	$(C_6H_5)_2CHCH_3$	1/2	3 2	0.5	1.4
	$(C_6H_5)_3CCH_3$	0	1	—	0.5
IV	$C_6H_5CH_2CH_2C_6H_5$	2	—	0.4	1.5
	$C_6H_5CH_2C_6H_5$	1	—	0.25	0.9
V	$C_6H_5CH_2CH_2C_6H_5$	2	—	0.35	1.4
	$(C_6H_5)_2CHCH(C_6H_5)_2$	1/2	—	0.3	1.0
VI	$C_6H_5(CH_2)_2C_6H_5$	2	0	0.4	1.5
	$C_6H_5(CH_2)_3C_6H_5$	2	1	0.8	2.2
	$C_6H_5(CH_2)_4C_6H_5$	2	2	0.9	2.9
	$C_6H_5(CH_2)_5C_6H_5$	2	2+2γ	1.2	2.7
VII	$C_6H_5C(CH_3)_3$	0	9	—	2.4
	$(C_6H_5)_3CCH_3$	0	1	—	0.5
VIII	$(C_6H_5)_2CH_2$	1	0	0.25	0.9
	$(C_6H_5)_2CHCH_3$	1/2	3/2	0.5	1.4
IX	$(C_6H_5)_3CCH_3$	0	1		0.5
	$(C_6H_5)_3CH$	1/3	0	—	0.2

found by additivity in the calculation involving the number of benzene rings in the hydrocarbon molecule. The maximum deviation was noted in the case of tetraphenylmethane. It is not excluded that the reactivity of aromatic rings of tri- and diphenylmethanes depends, to some degree, not only on the conjugation of the ring π-electrons and the aliphatic CH-bond σ-electrons, but also on the above-cited effect of mutual action of benzene rings separated by a carbon atom. Hydrogenation in diphenylmethane is exchanged at a slower rate than in diphenyl. Taking into account the suppositions made above, the conclusion that the reactivity of aromatic rings in reactions of electrophilic substitution of hydrogen is conditioned less by the σ,π-conjugation than by the π,π-conjugation, becomes more and more convincing.

The closure of the bond between the benzene rings of diphenylmethane provides some additional conjugation conditions both between the π-electrons of the aromatic rings and between them and the σ-electrons of the aliphatic CH-bonds of the methylene group. The reactivity of the substance rises very considerably. The isotope exchange of aromatic hydrogen atoms with liquid deuterium bromide is accelerated considerably. At the same time, the hydrogen atoms of the methylene group of fluorene exchange with liquid deuteroammonia at a rate that is seven orders of magnitude greater than the methylene group atoms in diphenylmethane [22, 23].

A comparison of the effect of the type of conjugation on the reactivity of hydrocarbons has a qualitative character since the concepts themselves about bond conjugation, in the form in which chemists usually employ them, are also qualitative [24].

The supposition about the existence of a dependence of reactivity of phenylated alkanes on the ratio between the number of aliphatic CH-bonds and of aromatic rings is, in general, confirmed by the experiments. Thus, while in the replacement of hydrogen atoms in methane or in ethane by phenyl groups, a progressive increase

of reactivity is possible owing to the mutual effect of the phenyl groups, the rate of exchange with deuterium bromide declines successively in the series: toluene > diphenylmethane > triphenylmethane (Table 2, group II), and in the series: ethylbenzene > 1,1-diphenylethane > 1,1,1-triphenylethane (group III).

Hydrogen is exchanged more rapidly in the aromatic rings of dibenzyl than in diphenylmethane (group IV), although the rings are closer to each other in the latter molecule. The results of the experiments with dibenzyl and tetraphenylethane (group V) is less clear.

The number of α-CH-bonds is fixed in group VI of symmetric diphenylalkanes, beginning with diphenylethane and finishing with diphenylpentane. Hence, the rate of hydrogen exchange in the aromatic rings depends on the β-CH-bonds: the rate of exchange rises in succession: diphenylethane < diphenylpropane < diphenylbutane $\approx$ diphenylpentane. The α-CH-bonds are absent in tert-butylbenzene and triphenylmethylmethane and the ratio between the number of β-CH-bonds and phenyl rings is different; the rates of exchange* are also different (group VII).

Like us, N.N. Lebedev [5] noted** the acceleration of the reaction (alkylation) in passage from diphenylmethane (0.092) to 1,2-diphenylethane (0.125) and 1,4-diphenylbutane (0.128). In the parentheses we showed the rate constants of the alkylation reaction with cyclohexyl chloride in nitrobenzene solution, expressed in min^{-1}. According to Lebedev, the deactivating effect of phenyl groups on each other is decreased by the increase of the distance of separation between them, this effect being dependent on the electronegativity of the phenyl group. This conclusion was based on the fact that the rate constant of alkylation of diphenyl, according to N.N. Lebedev's measurements, is somewhat less than double the rate constant for alkylation of benzene. However, as a rule, diphenyl reacts considerably more energetically than benzene in reactions of electrophilic substitution. Thus, the rate of hydrogen exchange with liquid deuterium bromide is more than three orders of magnitude higher [8], the rate of chlorination is more than 600 times higher [25, 26], that of nitration – 40 times [27, 28], bromination with Br^+ – 13 times higher [29]; acylation also proceeds more rapidly (in Friedel-Crafts reaction) for diphenyl than for benzene [30]. These facts contradict N.N. Lebedev's explanation.

Some of the results of this work may be compared with the data on the proton mobility of hydrogen atoms secured by the method of deuterium exchange with liquid deuteroammonia and with the solution of potassium amide in it [22, 31-33]. The hydrogen atoms of aliphatic CH-bonds in phenylated methanes are more mobile when the ratio CH/C_6H_5 is smaller. The hydrogen of the toluene CH_3-group exchanges only under catalysis with potassium amide ($k = 1.4 \cdot 10^{-3}$ sec^{-1} at 10° and $c_{KND_2} = 0.02$ N), while hydrogen of CH_2- and CH-groups in di- and triphenylmethane exchanges with ammonia without a catalyst. The rate constants at 120° are: $k = 7 \cdot 10^{-9}$ and $2 \cdot 10^{-7}$ sec^{-1}. Facts are known [32] which permit one to conclude that the mobility of hydrogen atoms in the CH-bonds and in β-position increases when the ratio between their number and the number of phenyl groups increases [comparison of hydrogen exchange in $C_6H_5C(CH_3)_3$ and $(C_6H_5)_3CCH_3$, $C_6H_5(CH_2)_4C_6H_5$ and $C_6H_5(CH_2)_3C_6H_5$].

One may approach the explanation of these regularities if one considers for the mechanism of hydrogen exchange [10, 33] that the deuterium exchange with an acid (and for other reactions of electrophilic substitution) is aided by an increase of electronegativity of the aromatic ring, while the deuterium exchange with a base (and metallation reaction) is aided by electropositivity of the hydrogen atom of the CH-bond. Consequently, the ring electronegativity rises with increased ratio of CH/C_6H_5, while the CH-bonds, removed from the ring, also affect this phenomenon but with a lesser weight. Conversely, the greater is the number of rings per one CH-bond, the more positively charged and the more easily protonizable is the hydrogen atom. Unquestionably the nature of these phenomena is more complex. It appeared not so long ago that the peculiarities of reactivity of alkylbenzenes were singularly explainable from the point of view of conjugation effects. Judging by the more recent publications [34, 35], one must also consider the steric factors, the difference in degree of solvation, etc., i.e., actually, the phenomenon is more multilateral than supposed earlier.

Along with this, in connection with our data on the mutual effect of atoms in phenylated alkanes, it should be noted that a recent communication [36] speaks of the hyperconjugation energy H of a monoolefin being expressible in the form of a sum: $H = aH_\alpha + bH_\beta + cH_\gamma + dH_\delta$, where a, b, c and d are numbers of hydrogen atoms

*The number of rings is fixed in group VIII and the number of either α- or β-CH-bonds is varied while, in group IX, the number of bonds of both types is varied with fixed number of the rings.

**Work of N.N. Lebedev was published four years after our preliminary paper [11] which is not cited by him.

in α-, β-, γ- and δ-positions relative to the double bond, while H_α, H_β, H_γ and H_δ – is an increment for each of the hydrogen atoms in these positions.

We express our gratitude to V. Aiksna, who participated in part of the experiments and to A.I. Korolev for his interest in the work.

SUMMARY

1. Experiments were run on deuterium exchange of liquid deuterium bromide with the following hydrocarbons: diphenylmethane, triphenylmethane, tetraphenylmethane, fluorene, dibenzyl, sym-tetraphenylethane, 1,1,1-triphenylethane, 1,3-diphenylpropane, 1,4-diphenylbutane and 1,5-diphenylpentane.

2. It was shown that the phenyl rings, separated by a hydrogen atom (in tetraphenylmethane) affect each other's reactivity.

3. The effect of π,π- and σ,π-conjugation on the reactivity of the aromatic ring was compared.

4. Facts are cited which indicate the existence of a dependence of reactivity of aromatic rings in phenylated alkanes on the ratio of the number of aliphatic CH-bonds in α- and β-positions and the number of phenyl groups; an explanation of this rule is proposed.

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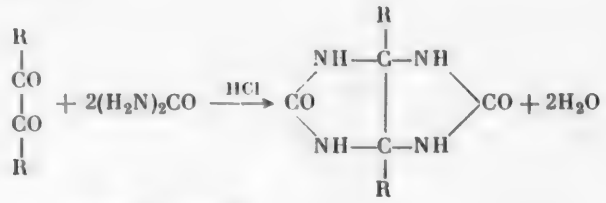
REACTION OF CYCLIC AND HETEROCYCLIC α-DIKETONES WITH UREA AND GUANIDINE

D.F. Kutepov, A.A. Potashnik, D.N. Khokhlov and V.A. Tuzhilkina

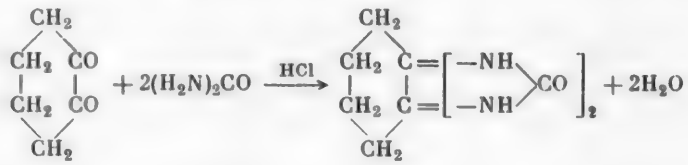
It is known that diureides of α-diketones are formed in the reaction of aliphatic and aromatic α-diketones with urea in an acid medium [1].



(R = alkyl, aryl).

We extended this reaction to o-quinones. Under similar conditions there were prepared diureides of phenanthrenequinone and its nitro derivatives in yields of 90% [2].

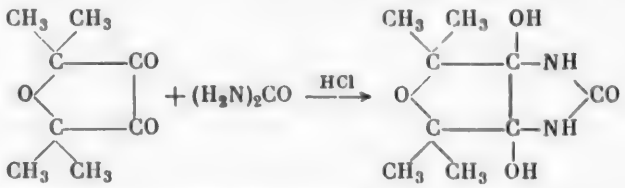
In the present work we examined the reaction of urea with cyclic and heterocyclic α-diketones. It was shown that cyclic α-diketones (1,2-cyclohexanedione and chloro-1,2-cyclohexanedione) react with urea similarly to the acyclic α-diketones and o-quinones.



The previously undescribed cyclohexanedione diureide and chlorocyclohexanedione diureide were prepared.

The chloro-1,2-cyclohexanedione necessary for the synthesis was prepared by us by chlorination of 1,2-cyclohexanedione in aqueous solution, from which precipitated the crystalline chlorocyclohexanedione with m.p. 54-55°. The location of the chlorine was not determined by us; however, this compound is not 3-chloro-1,2-cyclohexanedione, which has m.p. 123° [3].

The heterocyclic α-diketone, 2,2,5,5-tetramethyltetrahydrofuran-3,4-dione, prepared by us by the previously published method [4], reacts with urea under similar conditions with formation of,not a diureide, but a monoureide of tetramethyltetrahydrofurandione. The reaction evidently proceeds by the following equation.

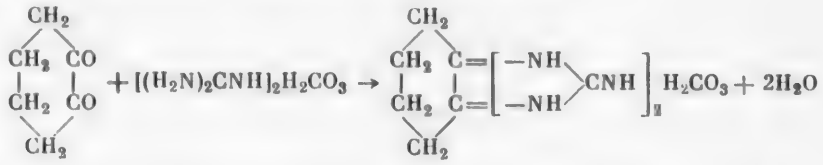


Such monoureides have been described in the literature [5].

It is known that the corresponding diguanides [6] are formed by the reaction of aliphatic and aromatic α-diketones and o-quinones with guanidine carbonate in an alkaline aqueous-alcoholic medium. However, the reaction of cyclic and heterocyclic α-diketones with guanidine has not been studied.

It was shown in the present work that cyclic α-diketones react with guanidine similarly to the acyclic α-diketones with formation of diguanides.

Cyclohexanedione diguanide carbonate was prepared by the reaction of 1,2-cyclohexanedione with guanidine carbonate in aqueous alcoholic medium, according to the equation



We failed to obtain the diguanide of chloro-1,2-cyclohexanedione since chloro-1,2-cyclohexanedione decomposed under the reaction conditions (in alkaline medium); guanidine does not react with α-diketones in neutral or acidic medium.

2,2,5,5-Tetramethyltetrahydro-3,4-furandione reacts with guanidine and forms, not a diguanide, but a monoguanide – tetramethyltetrahydrofurandione guanide.

EXPERIMENTAL

Cyclohexadione diureide. A hot solution of 4 g of urea in 25 ml of water, 4-5 drops of sulfuric acid were added to 2.5 g of 1,2-cyclohexanedione and the whole was refluxed for five minutes; a precipitate formed thereby and this was filtered off after cooling, washed with water and dried. 3.7 g (84.6%) of a colorless crystalline powder was obtained which, after recrystallization from water, had m.p. 319-320° (decomp.).

Found %: C 48.68, 48.99; H 5.50, 5.85; N 28.85, 29.12. $C_8H_{12}O_2N_4$. Calculated %: C 48.91; H 6.13; N 28.58.

Chlorocyclohexanedione diureide. Chloro-1,2-cyclohexanedione was first prepared by the following method. 10 g of 1,2-cyclohexanedione was dissolved in 40 ml of water. The solution was cooled with ice water and treated with chlorine with stirring. The resulting crystalline precipitate was filtered off, washed with ice water, and dried in air. 6 g of colorless crystalline substance was obtained with m.p. 53-55°. Yield: 46.1%.

Found %: C 39.73, 39.26; H 6.82, 6.68; Cl 18.73, 18.72. $C_6H_7O_2Cl \cdot 2H_2O$. Calculated %: C 39.50; H 6.04; Cl 19.45.

3.7 g (76.1%) of a colorless crystalline substance was obtained similarly from 3.7 g of chloro-1,2-cyclohexanedione and 4 g of urea dissolved in 30 ml of water, analogously to preparation of cyclohexanedione diureide. M.p. 270-271°.

Found %: C 42.36, 42.69; H 5.36, 5.49; N 23.27, 23.23; Cl 15.72, 15.66. $C_8H_{11}O_2N_4Cl$. Calculated %: C 41.65; H 4.81; N 24.29; Cl 15.38.

Tetramethyltetrahydrofurandione ureide. 2 g of 2,2,5,5-tetramethyltetrahydro-3,4-furandione and 2 g of urea were dissolved by heating in 5 ml of water, two drops of hydrochloric acid were added and the whole was heated under a reflux condenser for 30 minutes, whereby a colorless crystalline precipitate formed. The precipitate was filtered off after cooling, washed with water and dried. 2.4 g (88%) of a substance was obtained. It was recrystallized from alcohol. Decomposition point: 202-203°.

Found %: C 50.20, 50.39; H 8.30, 8.06; N 13.28, 13.25. $C_9H_{16}O_4N_2$. Calculated %: C 49.99; H 7.46; N 12.96.

Cyclohexanedione diguanide carbonate. A hot solution of 6.4 g of guanidine carbonate and 25 ml of water was added to a hot solution of 4 g of 1,2-cyclohexanedione in 50 ml of alcohol and the whole was refluxed for

2-3 minutes; a colorless crystalline precipitate was formed thereby, which was filtered off after cooling, washed with water and dried. 5.6 g (61.4%) of a colorless crystalline substance with decomposition point of 189-190° was isolated. The decomposition point failed to change after a recrystallization from water.

Found %: C 41.66, 41.88; H 7.07, 6.83; N 32.54, 32.81. $C_8H_{14}N_6 \cdot H_2CO_3$. Calculated %: C 42.19; H 6.26; N 32.81.

Tetramethyltetrahydrofurandione guanide. A hot solution of 7 g of guanidine carbonate in 40 ml of water was added to a hot solution of 6 g of 2,2,5-5-tetramethyltetrahydro-3,4-furandione in 20 ml of alcohol and the whole was heated under a reflux condenser for 20 minutes. The resulting precipitate was filtered off after cooling, washed with 30% alcohol and dried. 7.6 g of a white powder was isolated. Yield: 92.7%. It was recrystallized from water. Decomposition point: 225°.

Found %: C 50.17; H 8.00; N 20.23. $C_9H_{17}O_3N_3$. Calculated %: C 50.21; H 7.96; N 19.53.

SUMMARY

1. Cyclic α-diketones react with urea and guanidine similarly to the acyclic α-diketones and o-quinones, with formation of diureides and diguanides.

2. The heterocyclic α-diketone, 2,2,5,5-tetramethyltetrahydro-3,4-furandione reacts with urea and guanidine under similar conditions, forming the monoureide and the monoguanide.

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STUDIES IN THE FIELD OF CHEMISTRY OF FREE RADICALS OF THE HYDRAZINE SERIES

I. SOME DERIVATIVES OF α,α-DIPHENYL-β-PICRYLHYDRAZYL

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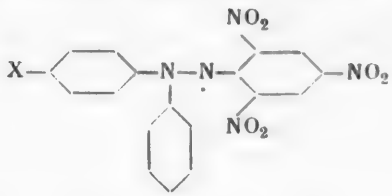
S.M. Kirov Ural Polytechnic Institute

The technique of the electronic paramagnetic resonance [1] is one of the physical methods permitting one to determine the presence of unpaired valence electrons in free radicals. Thus, for example, a series of stable hydrazine radicals, such as α,α-diphenyl-β-picrylhydrazyl [2, 3], α-9-carbazolyl-α-phenyl-β-picrylhydrazyl [3, 4], α,α-diphenyl-2,4-dinitro-6-sulfophenylhydrazyl [5] and some p,p'-substituted derivatives of α,α-diphenyl-β-picrylhydrazyl [6] have been studied by this method.

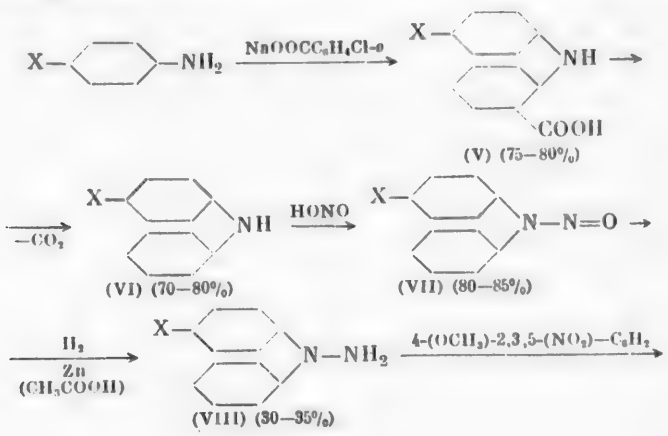
The application of the paramagnetic resonance method allows one to study the effect of various substituents in the free radical on the unpaired electron.

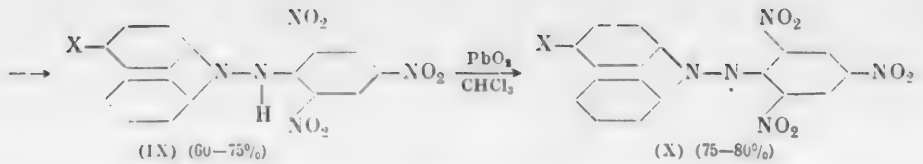
As objects of our study we chose monohalo derivatives of α,α-diphenyl-β-picrylhydrazyl (I) with substituents X in para position in the phenyl ring (II-IV).



X = H (I); F (II); Cl (III); Br (IV).

Two of these hydrazyls (II and III) were prepared for the first time. The synthesis of these compounds was accomplished by the following scheme:





(IX) (60—75%) (X) (75—80%)

Radical (IV), containing bromine as well as an unsubstituted radical, was prepared according to Goldschmidt [7].

The hydrazyls are soluble in chloroform with an intense permanganate color, and crystallize well from a mixture of chloroform and ether in the form of black-violet plates; they are not noticeably changed after prolonged storage in air.

The exchange interactions of the unpaired electron in respect to the presence of one or another halogen in para-position in the phenyl residue were examined by the method of electronic paramagnetic resonance in the radicals prepared by us. The measurements were done by the method of the network current devised by Zavoiskii [8].•

It is known that the form of the curve of paramagnetic resonance absorption is regarded as a characteristic of exchange interactions [10]. The form of the absorption curve is characterized by the relationship of the fourth moment to second: M_4/M_2. The moment of n-th order is equal to

$$M_n = \left[\frac{\int_{H=0}^{H=\infty} A(H) H^n dH}{\int_{H=0}^{H=\infty} A(H) dH} \right]^{1/n}$$

For Gaussian form of the line, the relation $M_4/M_2 = 1.32$. The considerable exchange interaction occurs if this value is close to 1.4 or above. Thus, for α,α-diphenyl-β-picrylhydrazyl it was found [11] that this value is equal to 1.44. It was established in a study of the superfine structure of this radical that the density of unpaired electrons is uniformly distributed between both nitrogen atoms [12] while in the carbazyl analog the electron density is greater at one of the nitrogen atoms [5]. Thus, it is possible to characterize the mobility and the peculiarities of the properties of unpaired electrons in any radical by a study of the exchange interactions.

The greater are the exchange interactions, the more mobile is the unpaired electron, as if it were delocalized, while, conversely, the smaller are the exchange interactions, the less mobile and more localized is the unpaired electron. The width of the lines of the curve of paramagnetic resonance may thus serve as a characteristic of the degree of delocalization of the unpaired electron [1, 6]: the narrower is this width, the greater is the delocalization (greater possibilities for conjugation with π-electrons of the rings), and, conversely, the wider is the curve, the smaller is the delocalization (less possibility for conjugation with π-electrons of the rings).

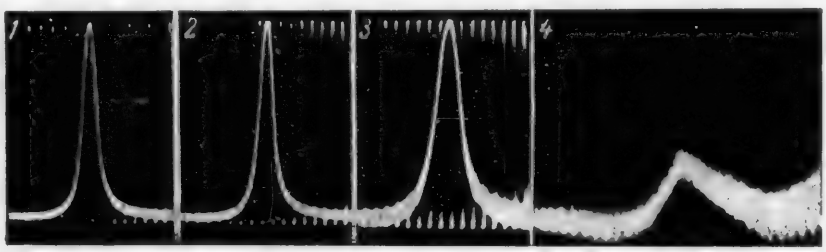


Fig. 1. Oscillograms of curves of paramagnetic absorption by radicals: 1) α,α-diphenyl-β-picrylhydrazyl (1); 2) α-p-chlorophenyl-α-phenyl-β-picrylhydrazyl (3); 3) α-p-bromophenyl-α-phenyl-β-picrylhydrazyl (4); 4) α-p-fluorophenyl-α-phenyl-β-picrylhydrazyl (2).

•Detailed data on measurement of paramagnetic resonance in compounds which are described in this paper are given in [9].

The photographs of the oscillograms of resonance absorption curves for these radicals are given in Fig. 1. The measured values of g-factor, width of the curve between points of maximum slope ΔH, the ratio of moments M_4/M_2, as well as values of A, proportional to the imaginary part of the susceptibility f", are given in Table 1. The ratio of the fourth moment to the second was determined by numerical integration of the experimental curve of absorption.

TABLE 1

Substituents X	g-Factor	M_4/M_2	ΔH (oersteds)	A
H	2.0042 ± 0.0004	1.43 ± 0.02	1.0 ± 0.15	300
Cl	2.001 ± 0.001	1.42 ± 0.02	1.2 ± 0.15	290
Br	2.002 ± 0.002	1.40 ± 0.02	2.2 ± 0.15	170
F	2.000 ± 0.004	Weak line	4.1 ± 0.5	20

As is evident from the data in Table 1 and in the photographs above taken from the oscillograms, the greatest exchange interaction occurs with the unsubstituted α,α-diphenyl-β-picrylhydrazyl (I), and the bromo derivative (IV) displayed a much smaller exchange interaction. For the α-p-fluorophenyl-α-phenyl-β-picrylhydrazyl (II) a minimum exchange interaction was found, which indicates the maximum stabilization (localization) of the unpaired electron at one of the nitrogen atoms of the radical (II).

In the work of Walter and his co-workers [6], in which data are cited about the paramagnetic resonance of p,p'-dihalo derivatives of picrylhydrazyl (I), the fluorine-containing radical also shows the smallest exchange interaction. Thus, once more, the rule is confirmed according to which the electron acceptor groups in the hydrazyl radical series act oppositely to their action in the triphenylmethyl radical series [13, 14].

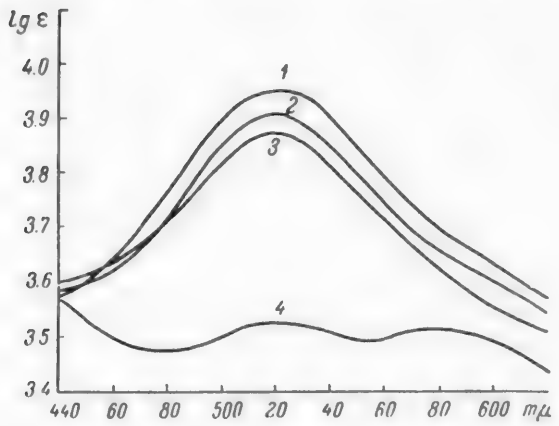
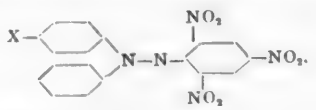


Fig. 2. Absorption spectra curves of free radicals:



Values of X: 1 — H, 2 — Br, 3 — Cl, 4 — F.

In addition to the study of the paramagnetic electronic resonance, it was interesting to study the absorption spectra of hydrazines and the radicals obtained from them both in ultraviolet and in visible regions. The spectra of the hydrazines (IX), with various substituents in the ultraviolet region of the spectrum, do not differ materially from each other. Similarly, the ultraviolet spectra of the radicals do not show differences among themselves (λ_{max} 330 to 335 mμ). All the hydrazines synthesized by us gave, in the visible part of the spectrum, some analogous shallow absorption curves without characteristic maxima.

A different picture was obtained for the radicals in the visible part of the spectrum. All the radicals had a maximum at λ 520 mμ, while the intensities of absorption differed considerably from each other depending on the substituent in the para-position. The greatest intensity was shown by the unsubstituted radical, the smallest – the fluoro derivative (Fig. 2).

The fact that a low intensity of the maxima in the absorption spectra for the fluoro derivative and the intensity of absorption maxima in the absorption spectrum of other derivatives are in the same order as the exchange interactions calls attention to itself, as possibly this is not purely accidental.

We suppose that a further study of the free radicals with various substituents by the method of electronic paramagnetic resonance will permit the development of a number of new aspects of electronic structure of these compounds.

EXPERIMENTAL

p-(X)-Diphenylaminecarboxylic acids (V). p-Chloro- and p-fluorodiphenylamine-o-carboxylic acids were prepared according to Ullmann [15, 16] by heating p-fluoro- and p-chloroaniline with sodium o-chlorobenzoate in the presence of finely divided copper. p-Fluorodiphenylamine-o-carboxylic acid was prepared in 82% yield; m.p. 196-200° (190-200° [16]); p-chlorodiphenylamine-o-carboxylic acid – in 80% yield; m.p. 175-177° (177° [15]).

p-Fluoro- and p-chlorodiphenylamines were prepared by decarboxylation of the corresponding p-(X)-diphenylamine-o-carboxylic acids by heating to above their melting points by 10-15° [15, 16]. p-Fluorodiphenylamine was prepared in 83% yield; m.p. 34-36° (36° [16]); p-chlorodiphenylamine – in 85% yield; m.p. 72-74° (74° [15]).

p-(X)-Diphenylnitrosamines (VII). 0.3 mole of concentrated hydrochloric acid was added with energetic stirring to a solution of 0.06 mole of p-(X)-diphenylamine in ethyl alcohol and, at a temperature of −2° to 0°, a solution of 0.12 mole of sodium nitrite in water was added with good cooling. The nitrosamine (VII) separated in the form of a light green precipitate after addition of a small amount of water. It formed almost colorless prisms after recrystallization from ligroin. The nitrosamines were soluble in the cold in alcohol, chloroform and ether. The solutions are colored green with concentrated hydrochloric acid. The analytical data and the properties of the nitrosamines are given in Table 2.

TABLE 2

Nitrosamines (VII)

Substituent (X)	Yield (in %)	Form of crystals	M.p.	Empirical formula	% N	
					found	calc.
F	84	Prisms with lettuce color	48-51°	$C_{12}H_9ON_2F$	12.86	12.95
Cl	80-85	Light-yellow prisms	84-87	$C_{12}H_9ON_2Cl$	12.32	12.07

α-p-(X)-Phenyl-α-phenylhydrazines (VIII). A 1.5-fold amount of zinc dust, relative to weight of (VII) was added to 0.04 mole of nitrosamine (VII) in alcohol. Glacial acetic acid was added in small portions with energetic shaking at −4° to 0°. The reaction was regarded as complete when a drop of the reaction mixture, added to concentrated hydrochloric acid, failed to give a green color in the solution.

The reaction mixture was heated to boiling and was filtered by suction from the solids. The mother liquor was distilled to $\frac{1}{4}$ of original volume and, after dilution with an equal volume of water, was treated with a large excess of concentrated hydrochloric acid. The hydrazine hydrochloride (VIII) precipitated from the cooled solution. This was separated and washed with a small volume of alcohol.

The hydrazine hydrochlorides were obtained in the form of colorless needles, after recrystallization from alcohol; they darkened after standing in air. They are difficultly soluble in cold alcohol, and readily soluble in warm water; they do not have a sharp melting point and decompose after preliminary darkening. The yields and the analytical data are given in Table 3.

TABLE 3

Hydrazine Hydrochlorides (VIII)

Substituent (X)	Yield (in %)	Empirical formula	% N	
			found	calc.
F	30-40	$C_{12}H_{11}N_2F \cdot HCl$	11.65	11.76
Cl	30-35	$C_{12}H_{11}N_2Cl \cdot HCl$	11.01	11.02

The hydrazine hydrochlorides (VIII) were treated at room temperature with 2-N sodium hydroxide solution for liberation of the free bases. The bases (VIII) were extracted with ether and the ethereal extracts dried over

solid sodium hydroxide. After the ether had been distilled off, the hydrazines were vacuum distilled; they were colorless oils, readily soluble in alcohol, chloroform and ether. The hydrazines dissolved in strong sulfuric acid with development of a dark blue color. The fluoro derivative had b.p. 166-167° (1 mm); yield: 30-40%. Chloro derivative had b.p. 186-188° (1 mm); yield: 30-35%.

The hydrazines were characterized in the form of their hydrazones with benzaldehyde and p-nitrobenzaldehyde. These compounds were obtained in quantitative yields. The properties and the analysis of the products are shown in Table 4.

TABLE 4

Hydrazones Y=H, Z=NO$_2$.

Substituent (X)	M.p.	Form of crystals	Empirical formula	% N found	% N calc.
F	Y 98-100°	Colorless needles	$C_{19}H_{15}N_2F$	9.91	9.65
	Z 164-166	Orange prisms	$C_{19}H_{14}O_2N_3F$	12.72	12.53
Cl	Y 119-121	Colorless needles	$C_{19}H_{15}N_2Cl$	9.32	9.15
	Z 150-151	Orange prisms	$C_{19}H_{14}O_2N_3Cl$	12.17	11.96

α-p-(X)-Phenyl-α-phenyl-β-picrylhydrazines (IX). A solution of 0.01 mole of 2,4,6-trinitroanisole (m.p. 58-59°) in chloroform was added at room temperature to 0.01 mole of p-(X)-diphenylhydrazine in chloroform. The chloroform was distilled from the dark red solution on a steam bath to $^1/_4$ of the original volume and two volumes of hot alcohol was added to the evaporated solution. Crystals of picrylhydrazines precipitated on cooling. These were separated and washed with a small volume of ether. Large red or orange crystals were obtained from glacial acetic acid, which were difficultly soluble in hot alcohol, ether and benzene and readily soluble in chloroform and hot acetic acid. The properties and the analyses of the hydrazines (IX) are shown in Table 5.

TABLE 5

Picrylhydrazines (IX)

Substituents X	Yield (%)	Form of crystals	M.p.	Empirical formula	Found (in %) C	Found (in %) H	Found (in %) N	Calc. (in %) C	Calc. (in %) H	Calc. (in %) N
F	73—75	Bright red prisms	177—179°	$C_{18}H_{12}O_6N_5F$	52.46	3.25	16.79	52.42	2.91	16.84
Cl	70—75	Red prisms	182—184	$C_{18}H_{12}O_6N_5Cl$	50.38	2.94	16.37	50.34	2.79	16.20
Br	60—65	Orange prisms	179—180	$C_{18}H_{12}O_6N_5Br$	—	—	15.00	—	—	14.77

Oxidation of hydrazines (IX) into radicals (X). 0.2 mole of lead dioxide and 0.01 mole of anhydrous sodium sulfate were added to 0.015 mole of p-(X)-diphenylpicrylhydrazine (IX) in dry chloroform. The reaction mixture was shaken for one hour. Then, the deep violet solution was separated from the solid. Chloroform was distilled from the filtrate under vacuum to $^1/_5$ the original volume. Two volumes of anhydrous ether was added to the residue. A black-violet crystalline precipitate of the radical formed from the resulting solution after many hours of standing; this was purified by reprecipitation with ether from a chloroform solution.

The hydrazyls were very difficultly soluble in alcohol and ether; readily soluble in chloroform and benzene. They rapidly passed into the hydrazines after reaction with an alcoholic solution of hydroquinone. The yields, melting points and analyses of the radicals are shown in Table 6.

TABLE 6

Picrylhydrazyls (X)

Substituent (X)	Yield (in %)	M.p.	Empirical formula	% N	
				found	calc.
F	80	163-164°	$C_{18}H_{11}O_6N_5F$	16.64	16.99
Cl	75-80	161-162	$C_{18}H_{11}O_6N_5Cl$	16.15	16.35
Br	80-85	153-154	$C_{18}H_{11}O_6N_5Br$	14.91	14.91

SUMMARY

1. Radicals of the hydrazine series were synthesized as follows: α,α-diphenyl-β-picrylhydrazyl (I), and its fluoro- (II), chloro- (III) and bromo- (IV) derivatives. Compounds (II) and (III) were prepared for the first time.

2. It was established during the study of exchange interactions of the unpaired electron by the method of paramagnetic resonance that the greatest exchange interactions are displayed by the unsubstituted hydrazyl (I), and the smallest – by the fluoro derivative (II). This indicates the considerably greater localization of the unpaired electron in this radical in comparison with the unsubstituted radical.

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PYRIDINE DYES – DERIVATIVES OF SECONDARY AMINES

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Pyridine dyes, derivatives of secondary amines, have not been studied sufficiently [1, 2]. In color and chemical properties they differ sharply from the corresponding derivatives of primary amines. A comparison of the data presented in Table 1 shows that the unsubstituted dye has a deeper color than the N-alkyl derivatives and that substitution of the hydrogens of the amine groups by phenyl radicals has no effect at all on the displacement of the absorption maximum.

TABLE 1

Absorption Maxima and Extinction Coefficients of Dyes in Ethyl Alcohol and in Ethyl Alcohol in the Presence of Hydrochloric Acid

Sample No.	$[C_6H_5N-(CH)_6-\underset{\displaystyle R_1=R_2=}{\overset{\displaystyle R_1}{\underset{\displaystyle R_2}{N}}}-C_6H_5]^+Cl^-$	Ethyl alcohol		Ethyl alcohol + HCl	
		λ_{max} (mμ)	$\varepsilon \cdot 10^{-4}$	λ_{max} (mμ)	$\varepsilon \cdot 10^{-4}$
1	H	487	4.0	487	8.8
2	CH_3	450	8.3	450	8.5
3	C_2H_5	442	6.6	442	6.8
4	C_6H_5	487	6.4	487	6.6

The derivative of aniline is readily hydrolyzed, acid suppresses the hydrolysis and in an acid medium the extinction coefficient is increased by a factor of two or more, while the absorption intensity of secondary amine derivatives hardly changes on the addition of acid. It was previously shown that the hydrolysis of pyridine dyes that were primary amine derivatives depended inversely on the basicity of the cation [3]. A comparison of the data in Table 1 indicates that the derivatives of secondary amines are not hydrolyzed. Table 1 shows the results of optical measurements on freshly prepared solutions; if the color intensity changes of the same dyes with time are followed in relation to the concentration, then it is seen that secondary amine derivatives are also hydrolyzed and the more rapidly the lower the basicity of the cation and the dye concentration.

As a comparison of the extinction coefficients shows, the N-methyl substituted dye is hydrolyzed less than the others and the diphenylamine derivative is strongly hydrolyzed. The facts presented indicate that the hydrolysis of secondary amine derivatives is also connected with the basicity of the cation and not only the character of the radical, but also its volume has an effect on the degree of it. The higher color of the N-ethylaniline derivative and its higher hydrolysis rate, in comparison with the methylaniline derivative, is probably caused by the greater steric hindrances in its molecule. The N-phenyl substituted dye we prepared did not differ in color from the aniline derivative, but the absorption intensity of its solutions was less under the same conditions than in the case of the latter. It is probable that replacement of the hydrogens at the nitrogen by phenyl radicals also destroys the planarity of the structure of the molecule, but to a lesser extent than with alkyl derivatives (Tables 1 and 2).

TABLE 2

Changes in the Extinction Coefficients of Dyes in Alcohol Solutions in the Presence of Hydrochloric Acid with Time (in hours) for Two Concentrations at 22°

Sample No.	R_1 R_2 $[C_6H_5-N-(CH)_5-N-C_6H_5]^+Cl^-$ $R_1 = R_2 =$	$\varepsilon \cdot 10^{-4}$					
		$C = 0.5 \cdot 10^{-4}$ M.			$C = 0.5 \cdot 10^{-5}$ M.		
		Time					
		0	5	20	0	5	20
1	H	10.2	—	5.0	8.8	—	1.8
2	CH_3	8.6	—	7.9	8.5	—	7.5
3	C_2H_5	6.9	5.8	3.7	6.8	—	2.5
4	C_6H_5	7.3	3.5	0.8	6.6	2.0	0.1

König [4] noted that, in the methylaniline derivative, the terminal units of the absorbing system are apparently the methyl groups; the benzene rings have a weak effect on the absorption of this dye and it hardly differs in color from alkylamine derivatives. However, in comparison with the dimethylamine derivative, the absorption maximum of the methylaniline derivative shows a bathochromic shift of 38 mμ [5]. Consequently, the benzene rings participate in the conjugation, but it is hindered.

In the hydrolysis of dyes that are primary amine derivatives, hydrogen chloride is eliminated to form yellow compounds, dianils of glutaconic aldehyde. Treatment of alcohol solutions of the secondary amines with alkali causes decolorization and in the spectra, bands appear in the near ultraviolet, which coincide almost completely with the bands of the corresponding monoanils of glutaconic aldehyde.

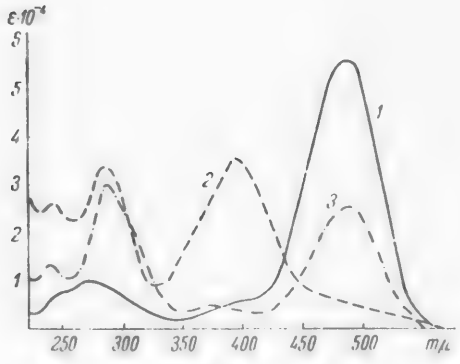


Fig. 1. Absorption spectra of dye – diphenylamine derivative: 1) in 96% ethyl alcohol; 2) the same + 40 equiv. NaOH; 3) the same + 40 equiv. NaOH + excess HCl.

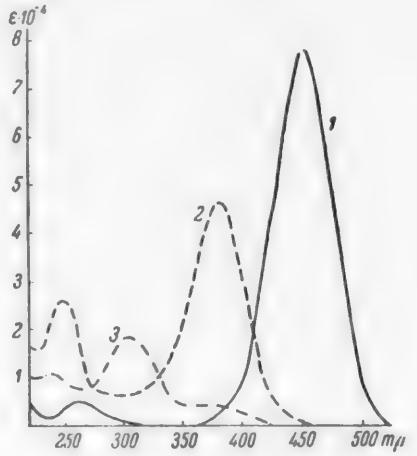


Fig. 2. Absorption spectra of dye – methylaniline derivative: 1) in 96% ethyl alcohol; 2) the same + 40 equiv. NaOH; 3) the same + 40 equiv. NaOH + excess HCl.

Figures 1 and 2 show absorption spectra of dyes that are diphenylamine and methylaniline derivatives in neutral and in alkaline media and after acidification of an alkaline solution. The addition of acid to a dilute solution partially restores the color of the diphenylamine derivative; in concentrated solutions, the color of the methylaniline derivative is also restored. Figures 3 and 4 show the spectra of the corresponding monoanils of glutaconic aldehyde. It can be postulated that, in the hydrolysis of secondary amine derivatives, carbinol bases are formed and these then decompose to the corresponding amines and monoanils of glutaconic aldehyde.

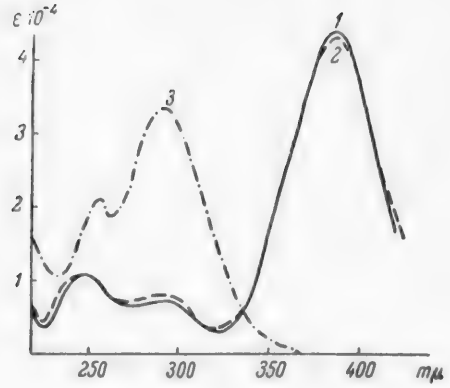


Fig. 3. Absorption spectra of the N-phenyl monoanil of glutaconic aldehyde: 1) in 95% ethyl alcohol; 2) the same + 40 equiv. NaOH; 3) the same + 40 equiv. NaOH + excess HCl.

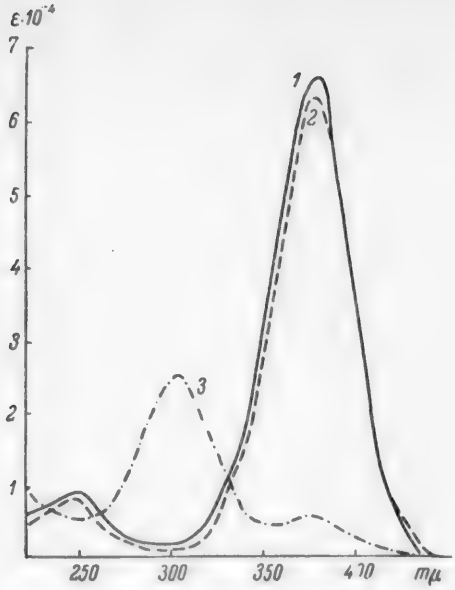
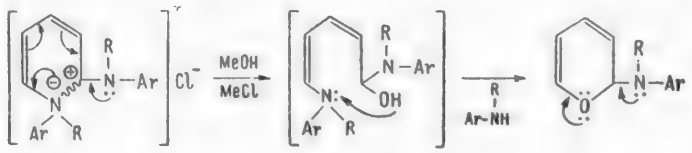


Fig. 4. Absorption spectra of the N-methyl monoanil of glutaconic aldehyde: 1) in 95% ethyl alcohol; 2) the same + 40 equiv. NaOH; 3) the same + 40 equiv. NaOH + excess HCl.

The carbinol base of the methylaniline derivative decomposed very rapidly due to the high basicity of the nitrogen of the amine group, to which the hydrogen of the hydroxyl migrated. The decomposition of the carbinol base of the diphenylamine derivative proceeds slowly and, after the addition of excess acid, the unchanged carbinol base again forms the dye. The monoanils are capable of condensing with amines in the presence of acids to form dyes, but this reaction does not occur in dilute solutions and there is partial decomposition of the monoanil into the corresponding amine and glutaconic aldehyde, while the corresponding bands appear in the spectra.

Elimination of the amine in the hydrolysis of dyes that are secondary amine derivatives, like their high color, is possibly caused by steric hindrance, which may be considerable only if the molecule of the pyridine dyes is assumed to have a cyclic structure [6]. Their hydrolysis may be represented by the scheme



In heterocyclic compounds of similar structure, the ring bonds (C—N; C—O) must be very much weakened due to the increase in the electron density at the α-carbon atoms; partial polarization of the ring bond causes the absorption of light in the visible region. Depending on the nature of the radicals at the nitrogen atom, the molecule may have either a planar structure or the aromatic rings destroy the planarity and the color is heightened as with N-alkyl substituted dyes.

The question of the formation mechanism and the structure of pyridine dyes has already been discussed [6]. New experimental data was obtained, confirming the hypothesis presented on the structure of the pyridine dyes. A special article will be devoted to this problem.

TABLE 3

Sample No.	Name of preparation	External form of crystals	λ_{max} mμ (in alcohol)	Yield (in %)	M.p.	Formula	% N	
							found	calc.
1	1,5-Bis-(N-ethylphenyl-amino)-pentadiene-1,3 chloride	Fine orange needles from acetone	442	30	102°	$C_{21}H_{25}N_2Cl$	8.35	8.21
2	1,5-Bis-(N-methyl-p-methylphenylamino)-pentadiene-1,3 chloride	Fine orange needles from acetone with ether	465	53	126	$C_{21}H_{25}N_2Cl$	8.30	8.22
3	1,5-Bis-(N-methyl-β-naphthylamino)-pentadiene-1,3 chloride	Dark-red needles with a bronze luster from acetone	467	48	134	$C_{27}H_{25}N_2Cl$	6.90	6.79
4	1,5-Bis-(N-phenylphenylamino)-pentadiene-1,3 chloride	Fine orange needles from 50% methyl alcohol + HCl	487	70	151	$C_{29}H_{25}N_2Cl$	6.41	6.39
5	1-(N-Ethylphenylamino)-pentadien-1,3-al-5	Lustrous yellow platelets from petroleum ether	380	10	67	$C_{13}H_{15}ON$	6.98	6.97
6	1-(N-Phenylphenylamino)-pentadien-1,3-al-5	Lustrous yellow needles from petroleum ether	387	40	103	$C_{17}H_{15}ON$	5.86	5.62

EXPERIMENTAL

The N-alkyl substituted dyes were prepared by the method of Zincke [1]. Besides the previously described methylaniline derivative, we synthesized and examined the N-methyl-p-toluidine [7] and N-methyl-β-naphthylamine [8] derivatives. Condensation of diphenylamine with the sodium enolate of glutaconic aldehyde [9] in the presence of hydrochloric acid yielded the N-phenyl substituted dye.

The secondary amine derivative dyes were readily soluble in methyl and ethyl alcohols and in acetic acid; they were purified by recrystallization from either acetone (in which they were slightly less soluble), alcohol acidified with hydrochloric acid or an acetone-ether mixture. Before analysis, the preparations were dried in vacuum over phosphorus pentoxide at 65°. The monoanils of glutaconic aldehyde were prepared by Zincke's method [1]. The N-phenyl monoanil was best prepared by hydrolysis of the corresponding dye with 5-8% sodium hydroxide solution in the cold or with gentle heating. The monoanils were purified by several recrystallizations from petroleum ether. The N-substituted monoanils of glutaconic aldehyde were readily soluble in many organic solvents. Data characterizing the preparations synthesized are presented in Table 3.

SUMMARY

1. Four N-substituted pyridine dyes and two monoanils of glutaconic aldehyde were synthesized. Four of the preparations obtained have not been described.

2. An examination was made of the absorption spectra of three N-substituted dyes and it was postulated that the nature of the color of the N-alkyl substituted dyes and their decomposition under the action of alkali was caused by steric hindrance, which may be considerable if a cyclic structure is assumed for pyridine dyes.

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HYDROGENATION OF SYLVAN ON NICKEL CATALYSTS IN THE LIQUID PHASE

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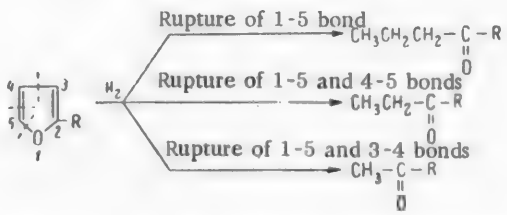
A series of experimental facts obtained by various authors leads to the conclusion that the hydrogenation of furan compounds may proceed in different ways depending on whether the reaction occurs in the liquid or the vapor phase. It was established that in the hydrogenation of sylvan and furyl alcohol on copper chromite in the liquid phase at 200-250°, the main reaction is the hydrogenolysis of the furan ring at the 1,2 and 1,5 ether bonds with the formation of almost equal amounts of pentanol-1 and pentanol-2 and pentanediols-1,2 and 1,5, respectively [1]. However, if sylvan is hydrogenated over copper chromite in the vapor phase at 275°, then the furan ring is hydrogenolyzed in only one direction, namely at the 1–5 C–O bond with the formation of methyl propyl ketone [2]. A Cu–ZnO catalyst behaves similarly and efficiently converts sylvan into pentanone-2 in the vapor phase at 325° [3].

Nickel deposited on aluminum oxide was found to be an active catalyst as regards hydrogenation of the furan ring in the liquid phase: in the hydrogenation of furan in an autoclave at 123-160°, tetrahydrofuran was obtained in an 86% yield [4]. However, this catalyst showed quite unsatisfactory activity in the hydrogenation of sylvan in the vapor phase at 275° [2]. Under these conditions tetrahydrosylvan and products of ring hydrogenolysis, aliphatic ketones, were obtained in not more than 20% yield. The main reaction products were substances with a high boiling point and also n-pentane and water. All this shows that the hydrogenation of the furan ring in the vapor phase over Ni–Al_2O_3 is accompanied by extensive decomposition of the furan ring and the formation of products with a more complex molecular structure. Of other nickel catalysts, we made a detailed examination of the hydrogenating properties in the vapor phase of a skeletal nickel-aluminum catalyst [5] and nickel deposited on zinc oxide [6].

Depending on temperature, the main reaction on a skeletal Ni–Al catalyst was either hydrogenation of the double bonds in the furan ring or hydrogenolysis of the furan ring with the formation of aliphatic alcohols or ketones. In contrast to other catalysts (Pt/C, Pd/C, CuO–Cr_2O_3), in the vapor phase a skeletal Ni–Al catalyst promoted so-called "conjugated" hydrogenolysis, i.e., cleavage of the furan ring simultaneously at the C–O and C–C bonds, as a result of which an alkylfuran molecule yields a molecule of an aliphatic alcohol or ketone and a hydrocarbon molecule. At 235-275°, the ring in α-alkyl and α-alkenylfurans is cleaved completely in three directions:



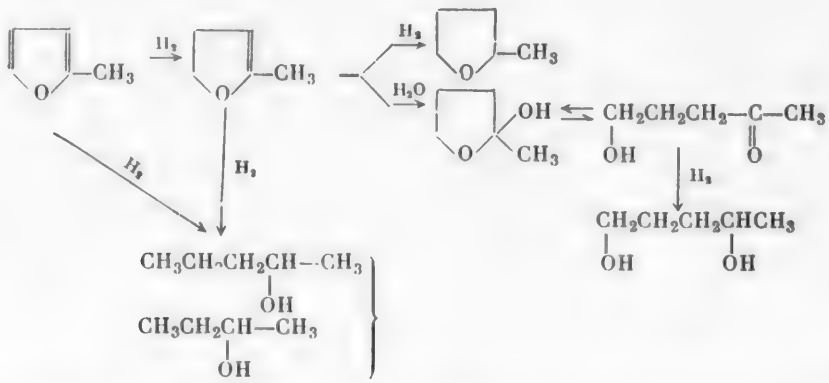
The 1–2 and 2–3 bonds, adjacent to the side substituent, were found to be stable under these conditions and hardly hydrogenolyzed at all. The dependence of the stability of the 3–4 and 4–5 C–C bonds on temperature is extremely interesting: with an increase in temperature, the relative strength of the 4–5 bond increases and that of the 3–4 bond decreases.

Nickel on zinc oxide has properties which differ sharply from those of the skeletal Ni—Al catalyst as regards hydrogenation of the furan ring. At 150° in the vapor phase, Ni—ZnO selectively hydrogenates a double bond in the side chain, leaving the multiple bonds in the furan ring untouched. At a higher temperature (250°), Ni—ZnO was found to be an extremely efficient catalyst in hydrogenolysis of the furan ring exclusively at the 1—5 C—O bond; alkylfurans form ketones in high yields. Thus, Ni—ZnO is unable to hydrogenate the furan ring in the vapor phase.

In the present work we investigated the hydrogenating capacity of a skeletal Ni—Al catalyst and Ni—ZnO in the liquid phase so as to elucidate the effect of the phase in which the reaction is performed on the hydrogenation of the furan ring. A comparison of the experimental data obtained with the rules we established earlier for the hydrogenation of furan homologs on the same catalysts in the vapor phase led to the conclusion that the hydrogenation of the furan ring on the same catalyst may proceed in different directions, depending on whether it occurs in liquid or the vapor phase.

Sylvan and α-propenylfuran were hydrogenated in an autoclave at 120-150° and a hydrogen pressure of 50-150 atmos in the presence of skeletal Ni—Al. The main reaction products were tetrahydrosylvan and α-propyltetrahydrofuran (85-95%), respectively.

An examination of the hydrogenolysis products of the furan ring in sylvan established that they consisted mainly of pentanediol-1,4, while the "normal" hydrogenolysis products, pentanol-2 and butanol-2, were obtained in considerably smaller amounts. The presence of pentanediol-1,4 in the hydrogenation products of sylvan indicates the extensive destruction of the sylvan molecule with the formation of water, which hydrolyzed the dihydrosylvan, formed as an intermediate compound, to give acetopropyl alcohol. The latter was then converted into pentanediol-1,4 by further hydrogenation [7].



In the simplest case, hydrogenolysis of sylvan with the formation of water must give n-pentane as the second product. However, the amount of this in the catalyzate was extremely small, which may be explained by condensation processes leading to compounds of complex molecular structure. Actually, the hydrogenation products always contained compounds, which decomposed even when distilled under reduced pressure.

Since a skeletal Ni—Al catalyst shows an increased tendency to add the elements of water to the double bond of dihydrosylvan, we hydrogenated sylvan in the presence of water and found that under these conditions almost equal amounts of tetrahydrosylvan and pentanediol-1,4 were formed. An insignificant amount (not more than 7%) of ring hydrogenolysis products, butanol-2 and pentanol-2, were obtained. These results show that the addition of the elements of water and hydrogen to the double bond of dihydrosylvan on the skeletal Ni—Al catalyst proceed at approximately the same rate and considerably faster than hydrogenolysis of the ring. The hydrogenation of sylvan in the presence of water almost completely eliminates the formation of high-boiling substances.

In addition to α-propyltetrahydrofuran, the hydrogenation products of α-propenylfuran on a skeletal Ni—Al catalyst contained in the high-boiling part mainly heptanediol-1,4, which was also formed, apparently, by the scheme indicated above.

Thus, the skeletal Ni—Al catalyst which has, at a certain temperature, a high activity for hydrogenation of the double bonds in the furan ring in both the liquid and the vapor phases, shows a profound difference as regards reactions connected with ring opening depending on the phase in which the hydrogenation is performed.

In the vapor phase, the furan ring is not only hydrogenated, but also hydrogenolyzed at the C−O and C−C bonds with the formation of aliphatic alcohols and ketones; in the liquid phase, ring opening is mainly connected with the addition of water to the double bond of 4,5-dihydro-2-alkylfuran with subsequent tautomeric conversion of the addition product into a keto alcohol and hydrogenation of the latter into an alkanediol-1,4. In the liquid phase a certain portion of the sylvan undergoes destructive hydrogenation with the formation of water and high-molecular compounds. Hydrogenolysis of the furan ring, leading to the formation of pentanol-2 and butanol-2 from sylvan, occupies a subsidiary position under these conditions. It is interesting to note that in both the liquid and the vapor phases at temperatures not exceeding 150°, hydrogenolysis of the furan ring on skeletal Ni−Al proceeds both at the 1−5 C−O bond and at the 1−5 and 4−5 bonds. The latter case yields an alcohol (or ketone), containing one carbon atom less in its molecule than in the molecule of the original alkylfuran.

Nickel on zinc oxide also shows an essential difference in its properties, depending on whether the furan ring is hydrogenated in the liquid or the vapor phase. While it is not able to hydrogenate the furan ring in the vapor phase [6], Ni−ZnO performs this reaction quite efficiently in the liquid phase. Thus, the hydrogenation of sylvan in an autoclave at 200-250° and a hydrogen pressure of 50-150 atmos yields tetrahydrosylvan in about 50% yield. In contrast to a skeletal Ni−Al catalyst, nickel on zinc oxide produces "normal" hydrogenolysis of sylvan at only the 1−5 C−O bond with the formation of pentanone-2 predominantly (35%) and only a small amount of pentanol-2 (5%). Complete hydrogenation of sylvan with cleavage of both C−O bonds and the formation of n-pentane and water occurs to a small extent (~4%).

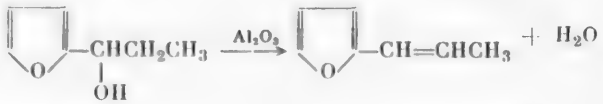
The formation of pentanone-2 on Ni−ZnO as the main ring hydrogenolysis product from sylvan in both the liquid and the vapor phase indicates that this catalyst has unusual properties. With other catalysts (copper, copper chromite and platinum), hydrogenolysis of sylvan in the vapor phase gives a ketone (pentanone-2) [2, 3], while in the liquid phase, only alcohols (pentanol-1 and pentanol-2) are formed, even at high temperatures (200-300°) [1, 8, 9].

The results of the present investigation lead to the conclusion that the direction of hydrogenation of the furan ring depends essentially on not only the nature of the catalyst, but also the nature of the phase in which the reaction is performed. The difference in the properties of skeletal Ni−Al catalyst and nickel on zinc oxide, which appears in the vapor phase in the hydrogenolysis of the furan ring ("conjugated" hydrogenolysis on Ni−Al and selective hydrogenolysis at the 1−5 C−O bond on Ni−ZnO), is also maintained in the liquid phase, though in this case hydrogenolysis occurs to an insignificant extent on Ni−Al. Both the catalysts investigated have a high activity in hydrogenation of the furan ring in the liquid phase, while Ni−ZnO is not able to hydrogenate the double bonds of the furan ring in the vapor phase.

EXPERIMENTAL

Starting materials. For the hydrogenation we used sylvan isolated from the technical product by distillation on an efficient column in the presence of sodium. It had the following properties: b.p. 63-64° (750), d^{20}_4 0.9120, $n^{20}D$ 1.4321.

α-Propenylfuran was obtained by dehydration of ethylfurylcarbinol over aluminum oxide at 350°.



As was noted previously [5], this also yielded a small amount of n-propylfuran. The dehydration product was dried with calcium chloride and distilled on a column. The α-propenylfuran, obtained in a 50% yield, had b.p. 132-133° (752 mm), d^{20}_4 0.9457, $n^{20}D$ 1.5098.

Catalysts. The skeletal nickel-aluminum catalyst was prepared by treating a nickel-aluminum alloy, containing 27% of nickel, with a 20% solution of sodium hydroxide. The ratio of the amounts of sodium hydroxide and alloy taken was such that about 10-15% of the total aluminum in the alloy was dissolved. The catalyst was washed free from alkali (reaction with phenolphthalein) and stored under a layer of distilled water.

Nickel on zinc oxide, containing 30% nickel, was prepared by coprecipitation of zinc and nickel hydroxides with ammonia solution from a combined solution of their nitrates. After being washed with water until the nitrate

ion disappeared (reaction with diphenylamine), the precipitate was filtered off, dried at 120° and formed into small cylinders. The catalyst was then reduced with hydrogen in a glass tube under the following temperature conditions: for the first four hours, the reduction was at 200°, for the following four hours at 250° and, finally, for a further four hours at 300°. This reduction method gave the most active samples of Ni–ZnO catalyst.

Liquid-Phase Hydrogenation of Sylvan and α-Propenylfuran on Skeletal Ni–Al Catalyst

Into a 1 liter autoclave was placed 400 g of sylvan and 30 g of Ni–Al catalyst. The initial hydrogen pressure at normal temperature was 120-150 atmos. The autoclave was heated to 150°, when the hydrogen was most rapidly absorbed in the temperature range 100-150°. The hydrogenation was concluded when the absorption of hydrogen ceased. The catalyzates obtained were separated from the catalyst, dried with potassium carbonate and distilled, first on a column at normal pressure and then with a still head under reduced pressure. From 4 kg of hydrogenated sylvan we obtained about 3.5 kg of tetrahydrosylvan, 25 g of butanol-2, 51 g of pentanol-2, 280 g of pentanediol-1,4 and about 140 g of intermediate fractions and high-boiling products.

Sylvan was hydrogenated in the presence of water, taken in an equimolar amount, under analogous conditions. The catalyzate contained tetrahydrosylvan (46%), pentanediol-1,4 (47%), butanol-2 (3%) and pentanol-2 (4%).

450 g of α-propenylfuran was hydrogenated in an autoclave at 120-130°. A 95% yield of α-propyltetrahydrofuran was obtained. Distillation of the high-boiling residue under reduced pressure yielded heptanediol-1,4 in amounts not exceeding 4%.

The properties of the products obtained in the hydrogenation of sylvan and α-propenylfuran on skeletal Ni–Al catalyst are presented in the table.

Hydrogenation Products of Sylvan and α-Propenylfuran over Skeletal Ni–Al Catalyst

Hydrogenation products	Boiling point (pressure in mm)	d^{20}_4	$n^{20}D$
Tetrahydrosylvan	79- 79.2° (750)	0.8582	1.4060
Butanol-2	98- 99.5 (755)	0.8076	1.3937
Pentanol-2	118-119 (755)	0.8087	1.4063
Pentanediol-1,4	104-105 (7)	0.9884	1.4475
α-Propyltetrahydrofuran	131-133 (750)	0.8562	1.4232
Heptanediol-1,4	133-135 (9)	0.9570	1.4513

Hydrogenation of Sylvan on Ni–ZnO Catalyst

500 g of sylvan was hydrogenated in an autoclave in the presence of 30 g of Ni–Al catalyst. The absorption of hydrogen proceeded quite slowly at 150° and therefore the hydrogenation temperature was raised to 250°. The catalyzate contained tetrahydrosylvan (50%), pentanone-2 (35%), pentanol-2 (5%), n-pentane (3-4%), and a slight high-boiling residue.

SUMMARY

1. The direction of hydrogenation of the furan ring depends on the nature of the catalyst and the phase in which the reaction is performed.

2. On a skeletal Ni–Al catalyst in the liquid phase at 120-150°, sylvan is not only hydrogenated to tetrahydrosylvan (90%) but also converted to pentanediol-1,4; at the same time, a certain fraction of the sylvan molecules undergo destructive hydrogenation with the formation of water and high-molecular compounds.

3. Hydrogenation of sylvan on skeletal Ni–Al at 120-150° in the presence of water leads to the formation of approximately equal amounts of tetrahydrosylvan and pentanediol-1,4 and insignificant amounts (~7%) of ring hydrogenolysis products, butanol-2 and pentanol-2.

4. Hydrogenolysis of the furan ring in sylvan in hydrogenation in the liquid phase on skeletal Ni–Al at 120-150° proceeds, as in the vapor phase, at the 1–5 C–O bond and at the 1–5 and 4–5 bonds with the formation of pentanol-2 and butanol-2, respectively.

5. In the liquid phase at 200-250°, nickel on zinc oxide is able to hydrogenate the double bonds of the furan ring (this reaction does not occur in the vapor phase) and hydrogenolyze the ring only at the 1–5 C–O bond with the formation of mainly pentanone-2 (in contrast to other catalysts).

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CATALYTIC REDUCTION OF PHENYLCARBINOLS INTO AROMATIC HYDROCARBONS

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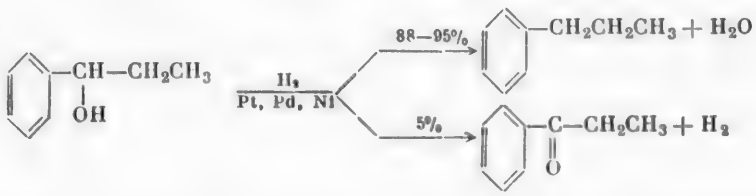
In previous work [1] we established that in the hydrogenation of alkylfurylcarbinols in the vapor phase on palladized charcoal and nickel on zinc oxide at 200-260°, there is selective reduction of the hydroxyl group with the retention of the multiple bonds in the furan ring, as a result of which, alkylfurylcarbinols are converted into α-alkylfurans. Raising the hydrogenation temperature facilitates the hydrogenolysis of the ring to a lesser extent on Pd–C and to a considerably greater extent on Ni–ZnO. At 250° on the latter catalyst, the α-alkylfurans, formed initially by reduction of the hydroxyl group of the alkylfurylcarbinols, are completely cleaved at the 1–5 C–O bond with the formation of the corresponding aliphatic ketones with the keto group in position 4. The capacity of the bond between the carbon atom and the hydroxyl group for rupture under the action of catalytically excited hydrogen depends on the presence of the furan ring adjacent to the hydroxyl group.

If, in compounds of the type R–CH(OH)–Alk, R represents an alkyl group, then the hydroxyl group is not reduced on Pd–C and Ni–ZnO, and there is dehydration of the alcohol to a ketone to a certain extent. The question arises as to what must be the chemical nature of R so that the hydroxyl group may be replaced by catalytically activated hydrogen?

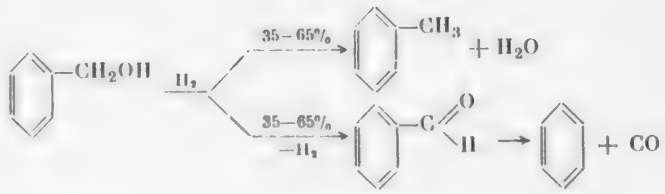
The results of the present investigation show that if R is a phenyl radical, then the hydroxyl group is reduced on Pt–C, Pd–C, Ni–ZnO and skeletal Ni–Al catalyst in the vapor phase at 250° and phenylcarbinols are converted into aromatic hydrocarbons. Thus, on all the catalysts investigated, ethylphenylcarbinol is converted into propylbenzene in 88-95% yields in the vapor phase at 250°. On skeletal Ni–Al catalyst, small amounts of benzene (3%) and toluene (3%) are formed in addition to propylbenzene, due to hydrocracking of C–C bonds in the side chain. Dehydrogenation of ethylphenylcarbinol into the corresponding ketone occurs to an insignificant extent.



Catalytic reduction of benzyl alcohol leads to the formation of a mixture of benzene and toluene in relative amounts, which depend on the nature of the catalyst used.

The formation of benzene does not proceed through the stage of toluene, since the latter is not demethylated into benzene on Pd–C and Ni–ZnO under the conditions of benzyl alcohol reduction. On the other hand, passing benzyl alcohol over Pd–C at 250° in the absence of hydrogen gives a mixture of benzene (75%) and toluene (25%), while benzaldehyde is only converted into benzene under these conditions. The reduction of benzyl alcohol into toluene apparently proceeds, in this case, due to hydrogen, formed in the dehydrogenation of the

alcohol into benzaldehyde. Thus, in the hydrogenation of benzyl alcohol there are two parallel reactions: reduction of benzyl alcohol into toluene and dehydrogenation of it into benzaldehyde with subsequent decarbonylation of the latter into benzene.



It is interesting to note that the dehydrogenation of benzyl alcohol into benzaldehyde occurs to the same extent as the reduction of the alcohol into toluene, while ethylphenylcarbinol is dehydrogenated to the ketone to a very small extent. The reason for this probably lies in the irreversibility of the decarbonylation of the aldehyde.

Aromatic hydrocarbons, obtained as a result of reduction on a palladium catalyst, are hydrogenated to a small extent into the corresponding cyclohexanes; reduction of the benzene ring does not occur on platinum and nickel catalysts.

In contrast to phenylcarbinols, pure aliphatic alcohols are not reduced to the corresponding hydrocarbons under the experimental conditions. Thus, on Pt–C, Ni–ZnO and skeletal Ni–Al at 250°, pentanol-2 is 50-65% dehydrogenated to the ketone and remains practically unchanged at this temperature on Pd–C. On Pt–C at 250°, heptanol-1 is not reduced to n-heptane, but is converted into n-hexane and carbon monoxide, decarbonylation products of the intermediate aldehyde formed.

Thus, like the effect of the furan ring in alkylfurylcarbinols, the effect of the benzene ring in phenylcarbinols weakens the bond between the carbon atom and the hydroxyl group and, due to this, the alcohol is reduced to the hydrocarbon on Pt, Pd and Ni very much more readily than it is dehydrogenated into the ketone; on the other hand, on these catalysts aliphatic alcohols only undergo dehydrogenation into ketones or aldehydes and the latter are readily decarbonylated under these conditions into the corresponding hydrocarbons.

EXPERIMENTAL

The benzyl alcohol used for the experiments had the following constants: b.p. 92-94° (12 mm), d^{20}_4 1.0465, $n^{20}D$ 1.5400. Ethylphenylcarbinol, synthesized by a Grignard reaction from benzaldehyde and ethyl bromide, had b.p. 90-92° (8 mm), d^{20}_4 1.0027 and $n^{20}D$ 1.5227.

Platinized charcoal, containing 15% Pt, was prepared by impregnating activated charcoal with chloroplatinic acid and reducing it in hydrogen at 300°. Palladized charcoal (10% Pd) was prepared by impregnating active birch charcoal with H_2PdCl_4 solution, followed by reduction with formalin in the presence of potassium hydroxide.

Nickel on zinc oxide (30% Ni) was obtained by coprecipitation of nickel and zinc hydroxides from a solution of their nitrates with ammonia. The catalyst was washed free from NO_3' ions, dried at 120° and reduced with hydrogen for twelve hours, while the temperature was gradually raised from 200 to 300°.

The Ni–Al skeletal catalyst was prepared by treating an Ni–Al alloy, containing 27% Ni, with 10% NaOH solution so that only 10-15% of the total aluminum in it was removed from the alloy.

Benzyl alcohol and ethylphenylcarbinol were hydrogenated in a flow system at 250° and normal pressure with a volume rate of 0.1 $hour^{-1}$. 100 g of substance was taken for each experiment. The catalyzates obtained were distilled on an efficient column.

The high-boiling fraction (180-220°) yielded a semicarbazone, which melted at 172-173° after recrystallization from ethyl alcohol. Consequently, this fraction contained propiophenone. The table gives the results of reducing benzyl alcohol and ethylphenylcarbinol on various catalysts at 250°.

Products of Catalytic Hydrogenation of Benzyl Alcohol and Ethylphenylcarbinol at 250°

Starting materials	Catalysts	Hydrogenation products
Benzyl alcohol	Pt–C	Benzene (60%), toluene (40%)
	Pd–C	Benzene (45%), toluene (30%), cyclohexane (20%), methylcyclohexane (5%)
	Ni–ZnO	Benzene (45%), toluene (55%)
	Ni–Al	Benzene (35%), toluene (65%)
Ethylphenylcarbinol	Pt–C	Propylbenzene (93%), propiophenone
	Pd–C	Propylbenzene (92%), propylcyclohexane (3%)
	Ni–ZnO	Propylbenzene (90%), propiophenone
	Ni–Al	Propylbenzene (88%), benzene (3%), toluene (3%), propiophenone

SUMMARY

1. Ethylphenylcarbinol is reduced in the vapor phase at 250° on Pt–C, Pd–C, Ni–ZnO and skeletal Ni–Al to propylbenzene in 88-95% yields and is dehydrogenated to ethyl phenyl ketone to an insignificant extent.

2. Under the same conditions, benzyl alcohol is reduced to toluene (35-65%) and dehydrogenated into benzaldehyde; the latter is readily decarbonylated to benzene at 250°.

3. On platinum and nickel catalysts at 250°, aliphatic alcohols (pentanol-2 and heptanol-1) are not reduced to hydrocarbons, but are only dehydrogenated to pentanone-2 and heptanal, respectively, while the latter is decarbonylated to n-hexane under the experimental conditions.

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ISOTOPE EXCHANGE OF SULFUR AND THE STRUCTURE OF "DISULFOXIDES" (SULFONOSULFIDES)

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Over a number of years there has been a discussion in the literature [1, 2, 9] on the structure of the "disulfoxides," R–SO–SO–R' (I) or R–SO_2–S–R' (II). Largely on the basis of synthesis methods, it was at first postulated that these compounds had a disulfoxide structure (I) and they appeared in the chemical literature under this name. In recent years, in connection with the discovery of the antibacterial and the antibiotic properties of these substances [1, 2], interest in them has increased considerably and many new compounds of this class have been synthesized [3]; at the same time, an ever increasing amount of data (both purely chemical and physicochemical) has been presented in support of the sulfonosulfide or the thiosulfonate configuration (II).

Previously [4], we measured the dipole moments and the vibration spectra of a large group of thiosulfonic esters and also arrived at the conclusion that "disulfoxides" have a sulfonosulfide structure (II).

In the present work a tracer method was used to study the problems of the structure and reactivity of these compounds. Up to now tracer methods have not been used in investigating this interesting and important class of substances. With the aid of this method, we hoped to obtain further information on the structure of thiosulfonic esters and also on their reactivity with respect to other sulfur-containing compounds. A study of the mechanism of the interaction of thiosulfonic esters with model substances, containing sulfhydryl and disulfide groups, not only may give information on the effect of structure on the reactivity, which is of general theoretical interest, but also may throw light on the mechanism of the antibacterial action.

In connection with this, three lines were followed in the work. A study was made of the isotope exchange of sulfur between various thiosulfonic esters on the one hand and elementary radioactive sulfur, on the other. A study was made of exchange of RS groups between various thiosulfonic esters, on the one hand, and labeled disulfides, on the other. Finally, a study was made of the conditions under which thiosulfonic esters react with mercaptans.

EXPERIMENTAL

Synthesis of Compounds Labeled with S^{35}

The allyl ester of allylthiosulfonic acid (pseudoallicin), labeled in the sulfide sulfur atom, $C_3H_5SO_2-\overset{*}{S}-C_3H_5$, was obtained by the reactions

$$C_3H_5SO_2Cl + Na_2\overset{*}{S} \rightarrow C_3H_5SO_2-\overset{*}{S}Na + NaCl$$

$$C_3H_5SO_2\overset{*}{S}Na + C_3H_5Br \rightarrow C_3H_5SO_2\overset{*}{S}C_3H_5 + NaBr$$

Freshly distilled (73-75° at 12-13 mm) allylsulfonyl chloride, synthesized by procedure [1], was added dropwise (with vigorous stirring) to an alcohol solution of labeled sodium sulfide cooled to 10-12°. The latter was prepared by absorbing labeled hydrogen sulfide in an alcohol solution of sodium hydroxide or by dissolving 1-2 mg of radioactive sulfur (5-10 mC) in sodium sulfide solution. When the sulfonyl chloride had been added, the mixture was stirred and heated (about two hours) on a water bath. Then, without isolation of the labeled sodium allylthiosulfonate, freshly distilled allyl bromide, dissolved in acetone, was added to the reaction mixture

in the cold. After standing at room temperature for 24 hours, the mixture was poured into water to deposit on the bottom of the beaker a colorless (sometimes pale yellow) oil, which was extracted with ether. The solution was dried with fused calcium chloride, the ether evaporated in the cold and the oil kept in vacuum (1-2 mm) at room temperature. Analysis of the product for sulfur content gave the following results: found 17.5%, calculated 17.2%. The activity of the sulfide sulfur atom of the pseudoallicin was equal to the activity of the original sodium sulfide.

Diethyl disulfide $C_2H_5\overset{\bullet}{S}-\overset{\bullet}{S}C_2H_5$ and ditolyl disulfide $CH_3C_6H_4\overset{\bullet}{S}-\overset{\bullet}{S}C_6H_4CH_3$, labeled with radioactive sulfur, were synthesized by the procedure described previously [5] and had constants which agreed with literature data.

Labeled diphenyl disulfide $C_6H_5\overset{\bullet}{S}-\overset{\bullet}{S}C_6H_5$ was prepared by isotope exchange with elementary radioactive sulfur. A mixture of diphenyl disulfide (3 g) and radioactive sulfur (0.1 g, 5-10 mC) was sealed in an ampoule in an atmosphere of nitrogen and placed in a thermostat at 235° for 5-6 hours. The cooled ampoule was opened (no excess pressure was observed) and the liquid red mass transferred to a flask with a reflux condenser, with the addition of toluene (5-7 ml). Sulfuric acid (1:7) and zinc dust was added to the mixture, which was boiled to reduce the disulfide and the polysulfides formed to thiophenol. The radioactive hydrogen sulfide liberated at this point was trapped in copper sulfate solution. The toluene layer, containing labeled thiophenol, was separated from the aqueous one and to complete the separation, the latter was washed with a fresh portion (~5 ml) of toluene, which was added to the first. The toluene solution of thiophenol was shaken with aqueous sodium hydroxide (10%) and the alkaline solution of labeled sodium thiophenolate oxidized with potassium ferricyanide. Recrystallization from alcohol yielded pure labeled diphenyl disulfide (m.p. 60°) with constant activity, which did not change with subsequent recrystallization. The yield was 50-60% of the original preparation.

The methods of synthesizing and purifying and the characteristics of the bulk of the compounds (unlabeled), used in the present work, were described previously [4].

A summary of the results on the isotope exchange of sulfur between esters of thiosulfonic acids and elementary sulfur is given in Table 1. After exchange, the components of the mixture were separated by vacuum distillation (in the case of ethyl esters) or fractional crystallization from alcohol; they were identified by melting and boiling points and by analysis for sulfur content.

TABLE 1

System	Temperature	Time (hours)	Percent exchange
Ethyltoluenethiosulfonate – sulfur $CH_3C_6H_4SO_2—SC_2H_5+\dot{S}$	104°	4	0
	115	4	0
Tolyltoluenethiosulfonate – sulfur $CH_3C_6H_4SO_2—SC_6H_4CH_3+\dot{S}$	116	2	0
	170	3	0
Ethylethanethiosulfonate – sulfur $C_2H_5SO_2—SC_2H_5+\dot{S}$	100	5	0
	115	5	0
Phenylphenylthiosulfonate – sulfur $C_6H_5SO_2—SC_6H_5+\dot{S}$	165	3	0

The results on isotope exchange of sulfur between esters of thiosulfonic acids and disulfides are presented in Table 2.

For all the compounds, the activity of benzidine sulfate precipitates was determined. The experiments were carried out in sealed ampoules. The components of the ethyl ethanethiosulfonate – labeled diethyl disulfide system were separated by fractionation in vacuum: 27° (1-2 mm) – diethyl disulfide, $n^{20}D$ 1.5062; 123° (11-12 mm) – thiosulfonic ester, $n^{20}D$ 1.4981.

For the allyl allylthiosulfonate–diallyl disulfide system, the disulfide was distilled off under mild conditions

TABLE 2

System	Temperature	Time (hr)	Activity before exchange: ester	Activity before exchange: disulfide	Activity after exchange: ester	Activity after exchange: disulfide	Calculated activity at equilibrium: ester	Calculated activity at equilibrium: disulfide	Percent exchange
$C_3H_5SO_2—\overset{*}{S}C_3H_5 + C_3H_5S—SC_3H_5$	20°	2	4050	0	—	1834	1350	2700	67
$C_6H_5SO_2—SC_6H_5 + C_6H_5S—\overset{*}{S}C_6H_5$	23	2	0	640	0	643	213	426	0
	61	0.5	0	120	40	84	40	80	100
	65	0.25	0	640	206	410	213	426	100
$C_2H_5SO_2—SC_2H_5 + C_2H_5S—\overset{*}{S}C_2H_5$	25	5	0	1386	0	1380	462	924	0
	100	5	0	1386	0	1382	462	924	0
	162	1	0	2676	260	2150	892	1784	30
	170	3	0	1386	469	915	462	924	100

(30-31° at 1-2 mm) to leave the ester. Experiments on the exchange between phenyl benzenethiosulfonate and labeled diphenyl disulfide were performed in benzene (0.1 N). After evaporation of the solvent (in the cold), the components were separated by fractional crystallization from alcohol.

As the data in Table 2 show, isotope exchange of sulfur was observed in all the systems examined under certain conditions. To demonstrate that the radioactive isotope of sulfur was transferred from one molecule to another as a result of exchange of RS groups and not sulfur atoms, experiments were carried out on the exchange between a thiosulfonic ester and a disulfide with different R. Equimolecular amounts of tolyl toluenethiosulfonate and labeled diethyl disulfide were kept at 162° for 3.5 hours. The exchange of groups in the reaction mixture must have produced labeled ethyl toluenethiosulfonate.

$$CH_3C_6H_4SO_2—SC_6H_4CH_3 + C_2H_5—\overset{*}{S}—\overset{**}{S}C_2H_5 \rightarrow$$

$$CH_3C_6H_4SO_2—\overset{*}{S}C_2H_5 + CH_3C_6H_4S—\overset{**}{S}C_2H_5$$

By fractionation in vacuum, we isolated and identified ethyl toluenethiosulfonate: b.p. 115° (4 mm), $n^{20}D$ 1.5731; found %: S 29.3, calculated %: S 29.6. Consequently, the radioactive isotope of sulfur was transferred from the disulfide molecule to the thioester molecule together with the ethyl radical.

Table 3 shows the results of measuring the kinetics of the exchange of C_2H_5S groups between the ethyl esters of various thiosulfonic acids and labeled diethyl disulfide

$$R—SO_2—SC_2H_5 + C_2H_5\overset{*}{S}—\overset{*}{S}C_2H_5 \rightarrow RSO_2—\overset{*}{S}C_2H_5 + C_2H_5S—\overset{*}{S}C_2H_5.$$

The course of the exchange reaction was followed by the change in the activity of the diethyl disulfide, which was distilled off in vacuum and identified by the boiling point (27-30° at 1-2 mm) and the refractive index ($n^{20}D$ 1.5063). All the experiments were performed with equimolar mixtures of ester and disulfide at 162°. The rate constants of the isotope exchange were calculated by the formula for equimolar concentrations with allowance for the number of exchangeable sulfur atoms in the compounds examined:

$$k = -\frac{1}{t}\ln\left(\frac{3x}{x_0} + 2\right),$$

where t is time, x_0 is the activity of the original disulfide, and x is the activity of the disulfide after time t.

The experimental values of $\ln\left(\frac{3x}{x_0} + 2\right)$ gave a good, straight line when plotted against t and the value of k was found by graphical extrapolation.

TABLE 3

Rate Constants of Isotope Exchange with Labeled Diethyl Disulfide at 162°

Ethyl ester	$k \cdot 10^{-3}$
Ethanethiosulfonic acid $C_2H_5SO_2-SC_2H_5$	0.25
Benzenethiosulfonic acid $C_6H_5SO_2-SC_2H_5$	0.14
β-Naphthalenethiosulfonic acid $C_{10}H_7SO_2-SC_2H_5$	0.32
p-Bromobenzenethiosulfonic acid $BrC_6H_4SO_2-SC_2H_5$	0.41
p-Toluenethiosulfonic acid $CH_3C_6H_4SO_2-SC_2H_5$	0.44
p-Nitrobenzenethiosulfonic acid $NO_2C_6H_4SO_2-SC_2H_5$	1.05

The results of experiments on the reactions of thiosulfonic esters with mercaptans are presented in Table 4. Solutions of equimolar amounts of thiosulfonate and mercaptan in benzene or toluene were mixed and kept at a given temperature for a definite time. The mixture was then treated with 10% sodium hydroxide. In accordance with the expected reaction, $R-SO_2-SR' + R''SH \rightarrow RSO_2H + R''S-SR'$, the aqueous layer was analyzed for the sulfinic acid and mercaptan content and the benzene layer for the disulfide and thiosulfonate content.

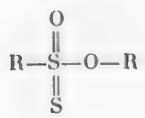
In the first three systems (Table 4), the corresponding sulfinic acids and disulfides were isolated and identified by the melting points and analysis for sulfur content. The other systems were only tested for mercaptan content with a buffered solution of lead acetate.

The allyl ester of allylthiosulfonic acid (pseudoallicin) and cysteine were reacted in an alcohol-water mixture. To determine to what extent the reaction presented above proceeded, we used labeled pseudoallicin. To a solution of pseudoallicin (0.9 g) labeled in the sulfide sulfur atom, in 10 ml of alcohol was added a solution of cysteine hydrochloride (0.8 g) in a mixture of alcohol (10 ml) and water (2 ml). After several minutes, a precipitate of silvery leaflets of S-thioallylcysteine began to form [6]. The radioactive isotope of the pseudoallicin, $C_3H_5SO_2-\overset{*}{S}C_3H_5$ (8000 imp) passed completely into the composition of the S-thioallylcysteine, $C_3H_5\overset{*}{S}-SCH_2-CHNH_2COOH$ (7932 imp/min).

DISCUSSION OF RESULTS

It is known that a sulfur atom connected to a carbon atom in an organic compound of the type R—S—R or RS—SR, etc., is not labile in the case of a comparatively simple R and does not exchange with elementary sulfur, even when heated to 200-250°. In addition, it is known that sulfur in different valence states is also incapable of exchange. Considering these circumstances, one would expect that in the esters of thiosulfonic acid investigated, regardless of whether they had structure (I) or (II), there would be no exchange with elementary sulfur under mild conditions. As the data in Table 1 shows, none of the compounds investigated exchanged with elementary sulfur when heated at 170°. These results completely exclude one of the possible configurations of thiosulfonic esters with a labile sulfur atom.

Bearing in mind the results of work [6, 7] on the exchange of RS groups between organic polysulfides and also between disulfides and mercaptans, one might expect that if the compounds investigated had the sulfonosulfide configuration (II) and not the disulfoxide one (I), then under certain conditions they would exchange R'S groups with corresponding disulfides.



The data presented in Table 2 very clearly indicate the presence of exchange between thiosulfonic esters and disulfides. Thus, as was shown above, these compounds do not exchange sulfur atoms but R'S groups.

TABLE 4

Starting materials		Reaction conditions	Products isolated		
thiosulfonic ester	mercaptan		sulfinic acid	disulfide	mercaptan
$CH_3C_6H_4SO_2-SC_6H_4CH_3$	$CH_3C_6H_4SH$	Benzene, 23°, 10 min Toluene, 83°, 1 hour	$CH_3C_6H_4SO_2H$	$(CH_3C_6H_4S)_2$	Not detected
$C_6H_5SO_2-SC_6H_5$	C_6H_5-SH	Benzene, 23°, 10 min	$C_6H_5SO_2H$	$C_6H_5-S-SC_6H_5$	
$C_3H_5SO_2-\overset{*}{S}C_3H_5$	Cysteine	Alcohol-water mixt. 20°, 15 min	—	$C_3H_5\overset{*}{S}-SCH_2-CHNH_2-COOH$	
$C_6H_5SO_2SC_6H_5$	C_2H_5SH n.-C_4H_9SH iso-$C_5H_{11}SH$	Benzene, 22°, 10 min	—	—	Not detected
$C_7H_7SO_2SC_7H_7$	C_2H_5SH n.-C_4H_9SH iso-$C_5H_{11}SH$		—	—	

The presence of exchange by R'S groups in the systems examined is an extremely weighty argument in support of the sulfonosulfide (II) configuration of thiosulfonic esters. We consider that, as a result of all the investigations, it can now be assumed proved that "disulfoxides" have the thiosulfonate or sulfonosulfide structure (II).

The data in Table 2 show that the capacity for exchange between thiosulfonic esters and disulfides depends, to a considerable extent, on the nature of the radicals R and R'. Allyl allylthiosulfonate (pseudoallicin) exchanges C_3H_7S groups with allyl disulfide even at room temperature; similar compounds with phenyl radicals exchange C_6H_5S groups with gentle heating (50-60°) and derivatives with ethyl radicals exchange only at ~160°.

Ethyl esters of different thiosulfonic acids, $R-SO_2-SC_2H_5$, exchange C_2H_5S groups with labeled diethyl disulfide (Table 3) under approximately identical conditions; the exchange proceeds at a measurable rate at 162°. All the observed variations in the rate constants of isotope exchange approximately fall within one order.

A comparison of the data in Tables 2 and 3 leads to the conclusion that the composition and structure of the radical R', forming part of the group R'S, has a considerably greater effect on the reactivity of the system RSO_2-SR' + $+ R'\overset{*}{S}-\overset{*}{S}R'$, than the radical attached to the sulfone group. We should note that this result, which we obtained by studying the lability of groups in model systems, agrees with the data of Belous [8] from a study of the antibacterial properties of a series of esters of thiosulfonic acids. It was shown that replacement of an allyl radical by a phenyl adjacent to the sulfonyl group, $C_3H_5SO_2-SC_3H_5$ and $C_6H_5SO_2-SC_3H_5$, had hardly any effect on the antibacterial activity, while a similar replacement of an allyl radical by a phenyl in the R'S group resulted in a compound of low activity. However, data on the effect of radicals on the reactivity of thiosulfonic esters is as yet far from sufficient for drawing more thorough conclusions.

We were unable to detect any similar effect of radicals on the reactivity of thiosulfonic esters with mercaptans since all the systems investigated (Table 4) reacted very rapidly at room temperature, regardless of the composition and structure of R and R'.

The exchange of RS groups between thiosulfonic esters and disulfides observed in the present work is extremely interesting, especially in connection with the antibacterial activity of thiosulfonic esters.

The problem of the mechanism of the antibacterial action of these compounds is discussed in the literature; however, it remains far from clear. Some authors [1, 2], basing their ideas on the reactions of thiosulfonic esters with mercaptans and compounds containing sulfhydryl groups

(cysteine and glutathione), have postulated that the antibacterial action consists of blocking the sulfhydryl groups of a metabolite according to the reaction

$$RSO_2—SR' + R''SH \rightarrow RSO_2H + R''S—SR'.$$

This causes disruption of metabolic processes in the bacterial cell.

The results of the present work indicate that thiosulfonic esters may react not only with sulfhydryls, but also with the disulfide groups of compounds, and, apparently, with the disulfide bonds of protein molecules. Therefore, the mechanism of the antibacterial action of thiosulfonic esters is probably very different to what was postulated previously.

On the basis of the results of the present work, in investigations on the antibacterial and antibiotic activity of thiosulfonic esters, it is necessary to consider possible reactions with the disulfide groups of protein.

SUMMARY

A tracer method was used for studying the structure and reactivity of thiosulfonic esters. It was shown that thiosulfonic esters do not exchange with elementary sulfur when heated to 170°.

The exchange of RS groups between thiosulfonic esters and organic disulfides was observed. It was decided that "disulfoxides" have a sulfonosulfide structure.

An investigation was made on the effect of the composition and structure of the radical on the exchange capacity of thiosulfonic esters with disulfides and mercaptans.

Conclusions were drawn on a possible mechanism for the antibacterial action of sulfonosulfides.

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INVESTIGATIONS IN THE FIELD OF THIOCARBANILIDE DERIVATIVES

I. SYNTHESIS OF SULFAMIDO-, CARBOXY- AND SULFO-SUBSTITUTED DERIVATIVES

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In recent years a large number of different thiourea derivatives have been synthesized and a wide investigation made of their antibacterial and, in particular, antituberculous properties [1-6]. Among the derivatives of thiourea, the sulfonamide and carboxy derivatives have been studied very little. The purpose of the present work was to fill in this gap.

We prepared diarylthiourea derivatives by one of the following methods.

1. $2RNH_2 + CS_2 \rightarrow RNHC(=S)NHR + H_2S$,

2. $2RNH_2 + CS_2 + I_2 + 2C_5H_5N \rightarrow RNHC(=S)NHR + 2C_5H_5N \cdot HI + S$,

3. $2RNH_2 + CS_2 \xrightarrow{S} RNHC(=S)NHR + H_2S$.

The best and most convenient method of preparing substituted arylthioureas was that starting from the appropriate amines and carbon disulfide in the presence of sulfur [7]. The arylthiocarbanilides synthesized are given in the table.

As the data in the table show, the arylthiocarbanilides were obtained in good yields. They formed crystals with characteristic melting points (with the exception of carboxy derivatives).

The figure shows the ultraviolet absorption spectra of alcohol solutions of five thiocarbanilides. The measurements were performed on an SF-4 spectrophotometer.

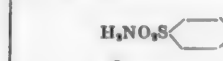
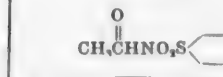
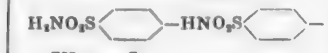
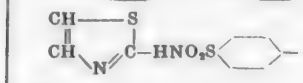
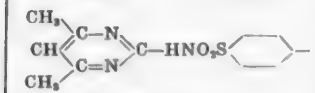
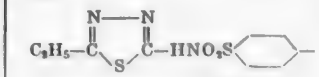
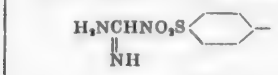
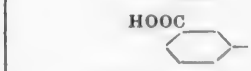
Solution concentrations: 1, 2 and 3 – $13.3 \cdot 10^{-5}$ mole/liter; 4 – $2.2 \cdot 10^{-5}$ mole/liter; 5 – $1.9 \cdot 10^{-5}$ mole/liter.

EXPERIMENTAL

Preparations 1-6 (table) were obtained by the method of Hugershoff [7]. We obtained preparations 7-9 starting from the appropriate amines, sodium hydroxide and carbon disulfide in methyl alcohol [1]. Preparations 10 and 11 were obtained previously by Fry in a less pure form by another method [8].

1,3-Di-(p-sulfamido)-thiocarbanilide. To a solution of 5 g of p-aminobenzenesulfonamide (streptocid album) in 150 ml of ethyl alcohol was added 0.5 g of sulfur and 5 ml of carbon disulfide. The mixture was heated on a water bath under reflux for ten hours until the evolution of hydrogen sulfide ceased. The solution had a yellow color at first and then the color almost disappeared. After cessation of hydrogen sulfide evolution, the mixture was filtered free from sulfur and part of the alcohol removed in vacuum on a water bath. The cooled solution deposited the thiocarbanilide as white, crystalline scales. The precipitate was filtered off, washed with water, alcohol and ether and dried in vacuum. The m.p. was 158° (with decomp.) and the yield 4.5 g (80.2%).

Thiocarbanilides of the General Formula RNHCNHR (S)

Sample No.	R	M.p.	Yield (%)	Empirical formula	Nitrogen content (in %) found	Nitrogen content (in %) calc.
1		165°	80	$C_{13}H_{14}O_4N_4S_3$	14.65, 14.78	14.50
2		180	96	$C_{17}H_{18}O_6N_4S_3$	11.85, 11.76	11.91
3		130	75	$C_{25}H_{24}O_8N_6S_5$	11.70, 11.90	12.07
4		194	92	$C_{19}H_{16}O_4N_6S_5$	14.95, 15.06	15.22
5		196	70	$C_{25}H_{30}O_4N_8S_3$	18.69, 18.79	18.73
6		187	65	$C_{21}H_{22}O_4N_8S_5$	18.35, 18.51	18.36
7		189	91	$C_{15}H_{18}O_4N_8S_3$	23.57, 23.68	23.83
8		142	64	$C_{13}H_{12}O_4N_6S_3$	19.25, 19.07	19.27
9		Does not melt	80	$C_{13}H_{10}O_6N_2S_3Na_2$	6.32, 6.59	6.48
10		Above 300	69	$C_{15}H_{12}O_4N_2S$	8.34, 8.44	8.86
11		Does not melt	62	$C_{15}H_{12}O_4N_2S$	8.51, 8.66	8.86

1,3-Di-(p-sulfoacetylamino)-thiocarbanilide. From 10 g of sulfanilacetamide (albucid) we obtained 10.5 g of 1,3-di-(p-sulfonacetamidophenyl)-thiocarbanilide (95.6%). The preparation was a crystalline product with a pale yellow color and m.p. 134° (with decomp.).

1,3-Di-(p-sulfanilamidosulfo)-thiocarbanilide. 10 g of p-sulfanilsulfanilamide (disulfan) was used for the reaction. The thiocarbanilide isolated appeared as a white crystalline powder with m.p. 130° (with decomp.). The yield was 8 g (75.2 g).

1,3-Di-(p-sulfamidothiazole)-thiocarbanilide. 10 g of 2-(p-aminobenzenesulfonamido)-thiazole (norsulfazol) was used. The thiocarbanilide obtained appeared as crystalline needles with m.p. 185° (with decomp.). The yield was 10 g (92.3%).

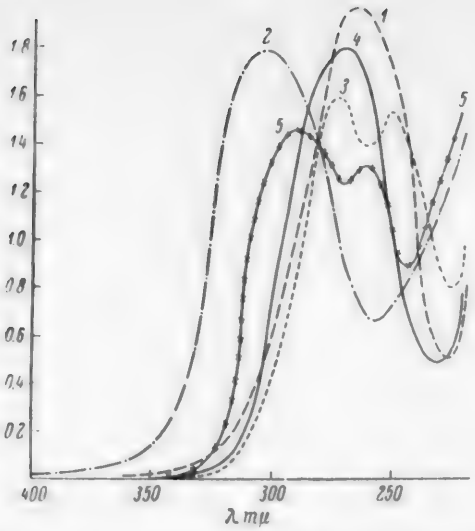
1,3-Di-(2-p-sulfamido-4,5-dimethylpyrimidine)-thiocarbanilide. 10 g of 2-sulfanilamido-4,6-dimethylpyrimidine (sulfodimesine) was used. The thiocarbanilide obtained appeared as white crystalline platelets with m.p. 188° (with decomp.). The yield was 7.5 g (69.7%).

1,3-Di-(2-p-sulfamido-5-ethylthiodiazole-1,3,4)-thiocarbanilide. The thiocarbanilide, obtained from 10 g of 2-(p-aminobenzenesulfamido)-5-ethylthiodiazole-1,3,4 (ethasol), appeared as white needles with m.p. 180° (with decomp.). The yield was 7 g (65.1%).

1,3-Di-(p-sulfoguanyl)-thiocarbanilide. 10 g of sulfanilguanidine (sulgine) was used for the reaction. The thiocarbanilide isolated formed a white crystalline powder with m.p. 182°. The yield was 10 g (91.5%).

1,3-Di-(p-sulfocyanamide)-thiocarbanilide. 10 g of sulfanilcyanamide (sulcymide) was used. The thiocarbanilide obtained formed white, crystalline needles with m.p. 140°. The yield was 7 g (63.6%).

1,3-Di-(p-carboxy)-thiocarbanilide. To a solution of 10 g of p-aminobenzoic acid in 250 ml of methanol



Ultraviolet absorption curves of thiocarbanilide derivatives: 1) 1,3-di-(p-sulfamido)-thiocarbanilide; 2) 1,3-di-(p-sulfoacetylamino)-thiocarbanilide; 3) 1,3-di-(p-sulfanilamidosulfo)-thiocarbanilide; 4) 1,3-di-(p-sulfamidothiazole)-thiocarbanilide; 5) 1,3-di-(p-sulfamido-4,5-dimethylpyrimidine)-thiocarbanilide.

and 3.5 g of sodium hydroxide was added 4.5 ml of carbon disulfide. The mixture was boiled under reflux on a water bath until the evolution of hydrogen sulfide ceased completely and this required about four days. On the second day, the precipitate was filtered off and the filtrate boiled gently for a further three days with the precipitate filtered off from it each day. The total weight of precipitate was 13 g. The precipitate, which was the sodium salt of the thiocarbanilide, was dissolved in 40 ml of water and the thiocarbanilide precipitated with 65 ml of 2 N hydrochloric acid to give a white, crystalline product. The precipitate was filtered off, washed with a small amount of water, then alcohol and ether, and dried in vacuum. It decomposed without melting. The yield was 7.2 g (62.4%).

1,3-Di-(m-carboxy)-thiocarbanilide. From 10 g of m-aminobenzoic acid we obtained 8 g (69.4%) of 1,3-di-(m-carboxyphenyl)-thiocarbanilide as a white, crystalline product. The m.p. was above 300°.

1,3-Di-(p-sulfo)-thiocarbanilide. 10 g of sulfanilic acid was used for the reaction. We obtained 10.5 g (80%) of the sodium salt of the thiocarbanilide as a white, crystalline powder. The sulfo derivative could not be obtained in the free state.

SUMMARY

Eleven sulfamido-, carboxy- and sulfo-substituted 1,3-thiocarbanilides were synthesized and of these, nine have not been described in the literature.

The ultraviolet absorption spectra of the thiocarbanilide derivatives synthesized were determined.

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INTERACTION OF PROPYLENE OXIDE WITH ORGANOCHLOROSILANES

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In one of our previous papers [1], we described the interaction of propylene oxide with organochlorosilanes, whereby, on the basis of the formation of α-chloropropionic acid by nitric acid oxidation of the hydrolysis products of the esters, we came to the conclusion that the oxide ring of the propylene oxide was opened on the side of the primary carbon atom.

In the present work we present the synthesis of eight previously undescribed β-chloropropoxyorganosilanes and also a further examination was made of the mode of opening of the oxide ring of propylene oxide during its interaction with organochlorosilanes.

Propylene oxide is an α-oxide with an unsymmetrical structure and its oxide ring can open in two ways during its reaction with organochlorosilanes.

$$CH_3{-}CH(O)CH_2 + R_nSiCl_{4-n} \rightarrow \begin{cases} \rightarrow R_nSi(OCH_2CHClCH_3)_{4-n} & \text{(a)} \\ \rightarrow R_nSi(OCHCH_2Cl)_{4-n} \\ \qquad\qquad | \\ \qquad\quad CH_3 & \text{(b)} \end{cases} \quad (1)$$

For an analogous reaction with ethylene oxide, Sauer and Patnode [2] suggested the following mechanism. Ethylene oxide is first converted into ethylene chlorohydrin due to hydrogen chloride, traces of which are always present in chlorosilanes.

$$H_2C(O)CH_2 + HCl \rightarrow HOCH_2CH_2Cl \quad (2)$$

Then the ethylene chlorohydrin reacts with the organochlorosilane by the equation

$$R_nSiCl_{4-n} + (4-n)HOCH_2CH_2Cl \rightarrow R_nSi(OCH_2CH_2Cl)_{4-n} + (4-n)HCl \quad (3)$$

Hydrogen chloride is regenerated and again reacts with the oxide by Eq. (2).

Propylene oxide reacts with organochlorosilanes by the same mechanism, but the problem is complicated by the fact that the oxide ring in it can be opened by hydrogen chloride in two ways: on the side of the primary or the secondary carbon atom. As a result, a mixture of isomeric halohydrins is obtained with a considerable predominance of the isomer corresponding to direction (a) [Eq. (4)], as was established by Petrov in his thorough investigations on this reaction [3].

$$CH_3{-}CH(O)CH_2 + HCl \rightarrow \begin{cases} \rightarrow CH_3CH(OH)CH_2Cl\ (90\%) & \text{(a)} \\ \rightarrow CH_3CHClCH_2OH\ (10\%) & \text{(b)} \end{cases} \quad (4)$$

Therefore, the second stage of the reaction, the interaction of the organochlorosilane with the chlorohydrin, proceeds in two directions [Eqs. (5) and (6)].

Formulas of compounds obtained	Starting materials				Yield (%)	B.p. (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		%Si		%Cl	
	alkyl(aryl)-halosilanes	d^{20}_4	n^{20}_D	b.p.					calc.	found	calc.	found	calc.	found
$CH_3Si\left[OCHCH_2Cl\right]_3$ (CH₃ on O)	CH_3SiCl_3	—	—	65.7°	66.9	143—144°(4)	1.4413	1.1464	74.86	74.61	8.68	8.63, 8.56	32.86	32.80, 33.00
$(CH_3)_3SiOCHCH_2Cl$ (CH₃ on CH)	$(CH_3)_3SiCl$	0.858	1.38	57—58	77.2	50—51 (30)	1.4226	0.9531	45.14	44.47	16.85	16.80, 16.77	21.27	21.31, 21.35
$C_2H_5Si\left[OCHCH_2Cl\right]_3$ (CH₃ on CH)	$C_2H_5SiCl_3$	1.238	—	97—98	80.2	131—132 (3)	1.4478	1.1320	79.49	79.84	8.32	8.36, 8.22	31.49	31.50, 31.42
$(C_2H_5)_2Si\left[OCHCH_2Cl\right]_2$ (CH₃ on CH)	$(C_2H_5)_2SiCl_2$	1.106 (d^{15}_4)	—	129	79.1	104—105 (3)	1.4455	1.0492	69.26	69.38	10.28	10.18, 10.23	25.95	25.98, 25.85
$(C_2H_5)_3SiOCHCH_2Cl$ (CH₃ on CH)	$(C_2H_5)_3SiCl$	0.897	1.43	144—145	59.9	73—74 (5)	1.4448	0.9476	59.03	58.62	13.45	13.54, 13.37	16.98	17.06, 16.96
$C_6H_5Si\left[OCHCH_2Cl\right]_3$ (CH₃ on CH)	$C_6H_5SiCl_3$	1.325 (d^{18}_4)	—	201.5	72.1	179—180 (3)	1.4892	1.1721	94.68	95.02	7.28	7.15, 7.23	27.57	27.59, 27.44
C_2H_5, H, C_6H_5, $OCHCH_2Cl$ (CH₃), Si	C_6H_5SiHCl (C_2H_5)	—	—	204—206	78.3	110—111 (3)	1.5011	1.0309	65.22	65.38	12.28	12.20, 12.32	15.50	15.63, 15.43
$Si\left[OCHCH_2Cl\right]_4$ (CH₃)	$SiCl_4$	1.523 (d^{0}_4)	—	59	84.2	163—164 (2)	1.4486	1.1950	89.72	90.20	6.98	6.90, 7.04	35.26	35.27, 35.40

$$R_nSiCl_{4-n} + (4-n)CH_3CH(OH)CH_2Cl \rightarrow R_nSi(OCH(CH_3)CH_2Cl)_{4-n} + (4-n)HCl \quad (5)$$

$$R_nSiCl_{4-n} + (4-n)CH_3CHClCH_2OH \rightarrow R_nSi(OCH_2CHClCH_3)_{4-n} + (4-n)HCl \quad (6)$$

As was already noted above, nitric acid oxidation of the hydrolysis products from the esters obtained forms an insignificant amount of α-chloropropionic acid; consequently, reaction (6) occurs. However, the formation of a very small amount of α-chloropropionic acid makes it possible to assume that the reaction between propylene oxide and organochlorosilanes proceeds mainly toward the formation of isopropylidene compounds, corresponding to formula (b) of Eq. (1), i.e., the reaction yields substances of normal and iso-structure [Eq. (1), directions (a) and (b)]. To confirm the accuracy of the latter proposal, we oxidized the hydrolysis products of the esters with nitric acid and also with chromic mixture.

Nitric acid oxidation of the hydrolysis products from the ester, obtained from methyltrichlorosilane and propylene oxide, yielded α-chloropropionic acid (in a small amount). A chromic mixture oxidation of the hydrolysis products from the same ester gave a good yield of chloroacetone, which confirms Eq. (5) or direction (b) in Eq. (1). Thus, in the interaction with organochlorosilane, the oxide ring of propylene oxide is opened in two directions [Eqs. (5) and (6)]. Consequently, the esters synthesized are mixtures of two substances with a predominance of the one which has the oxygen atom on the secondary and not on the primary carbon atom.

EXPERIMENTAL

Condensation of propylene oxide with methyltrichlorosilane. Into a three-necked flask, fitted with a mechanical stirrer, a reflux condenser, a dropping funnel and a thermometer, was placed 37.4 g of methyltrichlorosilane. 45.6 g of propylene oxide was added from the dropping funnel at such a rate that the temperature of the reaction mixture did not exceed 30°. After the introduction of all the oxide, the reaction mixture was heated for six hours on a water bath at 60° and left overnight. The reaction product was then vacuum distilled. We obtained 66.9 g (82.7%) of a substance with b.p. 143-144° (4 mm) with the following constants:

$n^{20}D$ 1.4413, d^{20}_4 1.1464, MR_D 74.61; calc. 74.86.

Found %: Cl 32.80, 33.00; Si 8.63, 8.56. $C_{10}H_{21}O_3Cl_3Si$. Calculated %: Cl 32.86; Si 8.68.

Propylene oxide was condensed similarly with the other organochlorosilanes (table).

Oxidation with nitric acid. Into a conical flask with 30 ml of 90% nitric acid, diluted with 20 ml of water, was introduced 20 g of the product obtained above. A vigorous reaction began soon and this was completed by heating to 40-45° for 40 minutes. The reaction mixture was diluted with 150 ml of water and extracted with ether. The extract was dried with anhydrous sodium sulfate, the ether removed and the residue distilled at normal pressure. The temperature increased continuously and it was not possible to obtain sharp fractions. However, at 184-185° (757 mm), we collected 0.6 g of substance, corresponding in properties to α-chloropropionic acid obtained by Henry [4]. The acid isolated had the following constants:

$n^{20}D$ 1.4815, d^{20}_4 1.3790, MR_D 22.36. $C_3H_5O_2Cl$. Calculated MR_D 22.41. Literature data [4]: b.p. 185°, d^9 1.386.

Oxidation with chromic mixture. Into a three-necked flask, fitted with a mechanical stirrer, a reflux condenser, a dropping funnel and a thermometer, was placed 25 g of sodium bichromate, 15 ml of water and 20 g of the substance obtained above. From the dropping funnel was added a solution of 30 g of concentrated sulfuric acid in 10 ml of water at such a rate that the temperature of the reaction mixture was 20-25° and the mixture was stirred continuously. When all the acid had been added, the mixture was stirred at room temperature for a further five hours and then extracted with ether. Distillation of the ether extract yielded 9 g of chloroacetone with b.p. 118-120°; the semicarbazone had m.p. 164° (with decomp.) (from alcohol) [5]. The structures of the other condensation products of propylene oxide and organochlorosilanes were established similarly.

SUMMARY

1. Condensation of propylene oxide with organochlorosilanes yielded eight previously undescribed β-chloropropoxyorganosilanes.

2. It was established that, in a reaction with organochlorosilanes, the oxide ring of propylene oxide is opened in two directions, on the side of the secondary and of the primary carbon atom. Therefore, the condensation products are mixtures of isomers with a predominance of that isomer with the oxygen on the secondary carbon atom.

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SYNTHESIS OF ALIPHATIC AMINO ACIDS FROM THIOPHENE DERIVATIVES

IV. 5-ACYL-(2-THIENYL)-ALKANOIC ACIDS AS STARTING MATERIALS FOR THE PREPARATION OF ALIPHATIC AMINO ACIDS

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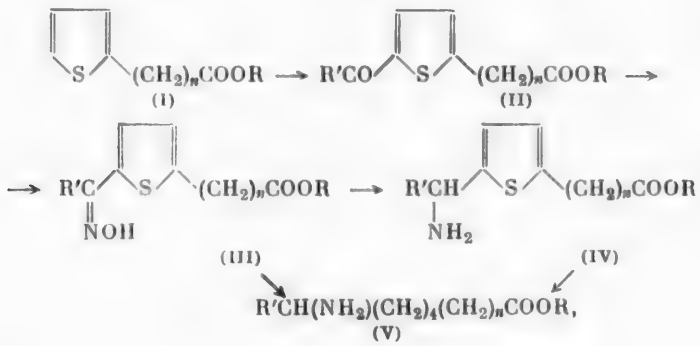
The higher aliphatic amino acids of the structure $RCH(NH_2)(CH_2)_nCOOH$, where R is alkyl, have been studied comparatively little, though they may be of interest as materials for polycondensation [1] or as derivatives for physiological investigations [2]. No general method for their synthesis is known; natural products have been used for the preparation of certain similar amino acids, for example, 10-aminoundecanoic acid [1, 2] was prepared from undecylenic acid, formed in the pyrolysis of castor oil.

We previously proposed a method, based on the reductive desulfurization (hydrogenolysis) of oximino- and amino acids of the thiophene series [3-8], which makes it possible to prepare amino acids of various types. The thiophene keto acids, which we used for the purpose previously [4], made it possible to synthesize only those amino acids in which the carbon atom bearing the amino group was connected to the alkyl, containing not less than four carbon atoms. This limitation was later partially eliminated by the use of oximes of aldehyde acids as starting materials [8].

In the present work, a synthesis is described for higher amino acids of the type given from oximes of keto acids (II) by the scheme



where R and R' are alkyls.

By this route, it is possible to prepare higher aliphatic amino acids, containing the amino group in a given position with respect to the carboxyl and having an alkyl residue with the required number of carbon atoms at the carbon atom connected to the amino group.

TABLE 1

Esters of keto acids of the thiophene series and their derivatives	B.p. (pressure in mm)	d_4^{20}	n_D^{20}	M.p.	Yield (%)	Empirical formula	%C		%H		%S	
							found	calc.	found	calc.	found	calc.
Methyl ester of δ-(5-acetyl-2-thienyl)-valeric acid	201° (10)	—	—	53—55°	71	$C_{12}H_{16}O_3S$	60.01, 59.83	59.97	6.84, 6.72	6.71	13.21, 13.58	13.34
Oxime	—	—	—	114—115	87.5	$C_{12}H_{17}O_3NS$	56.03, 56.08	56.44	6.73, 6.63	6.71	12.71, 12.45	12.56
Methyl ester of ε-(5-acetyl-2-thienyl)-valeric acid	212 (10)	—	—	41—42	87	$C_{13}H_{18}O_3S$	61.27, 61.43	61.38	7.26, 7.18	7.13	13.29, 13.35	12.61
Oxime	—	—	—	96—97	67	$C_{13}H_{19}O_3NS$	58.08, 57.90	57.97	7.26, 7.08	7.11	11.84, 12.03	11.91
Ethyl ester of γ-(5-propionyl-2-thienyl)-butyric acid	197—198 (10)	1.1050	1.5238	—	75	$C_{13}H_{18}O_3S$	61.64, 61.47	61.38	7.17, 7.02	7.13	13.02, 13.12	12.61
Semicarbazone	—	—	—	112—113	—	$C_{14}H_{21}O_3NS$	53.89, 54.13	54.00	6.52, 6.59	6.80	—	—
Methyl ester of ε-(5-propionyl-2-thienyl)-caproic acid	172—173 (1.6)	1.0959	1.5245	—	60	$C_{14}H_{20}O_3S$	62.72, 62.63	62.56	7.28, 7.29	7.51	11.87, 12.04	11.95

TABLE 2

Keto acids and their derivatives	M.p.	Yield (%)	Empirical formula	% C		% H		% S	
				found	calc.	found	calc.	found	calc.
δ-(5-Acetyl-2-thienyl)-valeric acid	83—84°	98	$C_{11}H_{14}O_3S$	59.05, 57.96	58.38	6.25, 6.17	6.24	14.01, 14.07	14.17
Oxime	182—183.5	96	$C_{11}H_{15}O_3NS$	54.58, 54.36	54.75	6.23, 6.08	6.27	13.42, 13.63	13.29
ε-(5-Acetyl-2-thienyl)-caproic acid	101.5—102	97	$C_{12}H_{16}O_3S$	59.98, 60.14	59.97	6.66, 6.64	6.71	12.86, 12.82	13.35
Oxime	101—102	—	$C_{12}H_{17}O_3NS$	56.47, 56.46	56.44	6.63, 6.76	6.71	12.71, 12.78	12.56
Semicarbazone	186—187	—	$C_{13}H_{19}O_3N_3S$	52.66, 52.42	52.50	6.52, 6.43	6.46	10.53, 10.62	10.77
γ-(5-Propionyl-2-thienyl)-butyric acid	71—72	84	$C_{11}H_{14}O_3S$	58.25, 58.42	58.38	6.00, 6.00	6.24	14.21, 14.62	14.17
High-melting oxime	128—129	95	$C_{11}H_{15}O_3NS$	54.78, 54.80	54.75	6.18, 6.23	6.27	12.95, 13.07	13.29
Low-melting oxime	91—93	—	$C_{11}H_{15}O_3NS$	54.59, 54.42	54.75	6.24, 6.20	6.47	13.08, 13.19	13.29
Semicarbazone	162.5—164	—	$C_{12}H_{17}O_3N_3S$	50.66, 50.53	50.86	5.84, 5.71	6.05	—	—
ε-(5-Propionyl-2-thienyl)-caproic acid	61—62	80	$C_{13}H_{18}O_3S$	61.41, 61.06	61.38	7.05, 6.98	7.13	12.66, 13.01	12.61
Mixt. of isomeric oximes	117—123	98	$C_{13}H_{19}O_3NS$	58.08, 58.06	57.97	7.22, 6.99	7.11	11.78, 11.52	11.91
Low-melting oxime	98—99	—	$C_{13}H_{19}O_3NS$	58.09, 58.12	57.97	7.13, 6.96	7.11	11.94, 11.98	11.91
Semicarbazone	155—156	—	$C_{14}H_{21}O_3N_3S$	53.84, 53.81	53.99	6.82, 6.84	6.80	10.11, 9.86	10.30

EXPERIMENTAL*

Esters of keto acids of the thiophene series (II) were synthesized by acylation of esters of appropriate ω-(2-thienyl)-alkanoic acids (I) (see [8] for the preparation) with acetyl chloride or propionyl chloride in the presence of stannic chloride by the usual method for the acylation of thiophene compounds. The oximes of these keto esters (III) were prepared by heating the keto esters in dilute methanol with a threefold excess of hydroxylamine hydrochloride, neutralized with the theoretical amount of sodium carbonate. The properties of the esters of the keto acids obtained and their derivatives are presented in Table 1. The melting points are given for substances recrystallized from dilute methanol.

Heating the esters of the keto acids (II) with dilute aqueous sodium hydroxide solution yielded the corresponding keto acids (II, R = H); they were recrystallized from dilute alcohol. The oximes of these keto acids (III, R = H) were prepared by heating the keto acids with a threefold excess of hydroxylamine hydrochloride in dilute aqueous sodium hydroxide solution, taken in an amount three times that required to neutralize the hydroxylamine hydrochloride [4]. The oximes were isolated from solution by acidification with hydrochloric acid. The same oximes were obtained by heating the oximes of the esters of the keto acids with alkali solution. Some of them melted over a wide range and, apparently, consisted of a mixture of stereoisomeric substances since the mother liquors from their recrystallization (dilute methyl alcohol) yielded products with a lower melting point than, but with the same elementary composition as, the high-melting oximes. The properties of the keto acids obtained and their derivatives are presented in Table 2.

In a series of cases, the oximino acids (III, R = H) were reduced with amalgamated aluminum [4] to yield the corresponding amino acids containing the thiophene nucleus (IV, R = H).

ε-[5-(1-Aminoethyl)-2-thienyl]-caproic acid (IV, R = H, R' = CH_3, n = 4). A solution of 9.1 g of unpurified oxime, obtained from ε-(5-acetyl-2-thienyl)-caproic acid (III, R = H, R' = CH_3, n = 4) in a mixture of 250 ml of warm methyl alcohol and 100 ml of water was added to amalgamated aluminum (prepared from 18.2 g of granulated aluminum). The mixture was shaken for 24 hours (continued

*E. Ya. Grens participated in the work.

overnight). The aluminum hydroxide was filtered off, and washed with hot water, the combined filtrates were evaporated to dryness in vacuum, and the residue was washed with 20 ml of alcohol. The weight of the dry substance was 1.72 g. After recrystallization from dilute acetone, the amino acid had m.p. 181-182°.

Found %: C 59.64, 59.65; H 7.95, 7.87; N 5.80, 5.80; S 13.42, 13.62. $C_{12}H_{19}O_2NS$. Calculated %: C 59.71; H 7.94; N 5.81; S 13.29.

The acetyl derivative of this amino acid was obtained by treating the amino acid with acetic anhydride in dilute sodium hydroxide solution and isolated by acidification of the solution with hydrochloric acid. The m.p. was 66-67.5° (from dilute methanol).

Found %: C 58.85, 58.91; H 7.16, 7.23; S 11.60, 11.35. $C_{14}H_{21}O_3NS$. Calculated %: C 59.33; H 7.47; S 11.32.

δ-[5-(1-Aminoethyl)-2-thienyl]-valeric acid (IV, R = H, R' = CH_3, n = 3) could not be obtained in a pure state for analysis; its acetyl derivative had m.p. 96.5-98° (from dilute methanol).

Found %: C 57.78, 57.88; H 7.17, 7.22; S 12.21, 12.32. $C_{13}H_{19}O_3NS$. Calculated %: C 57.96; H 7.11; S 11.91.

We previously noted that hydrogenolysis could be carried out more conveniently with the acetyl derivatives than with the amino acids themselves of the thiophene series [7]; therefore, in a series of cases, the esters of the amino acids, obtained by reduction of the oximino acids with amalgamated aluminum, were hydrolyzed and acetylated (without preliminary purification).

ε-[5-(1-Acetylaminoethyl)-2-thienyl]-caproic acid. 10.9 g of the oxime, obtained from the methyl ester of ε-(5-acetyl-2-thienyl)-caproic acid (III, R and R' = CH_3, n = 4), with m.p. 95°, was dissolved in a mixture of 450 ml of methyl alcohol and 100 ml of water. The solution was poured onto amalgamated aluminum (from 16.4 g of granulated aluminum). The mixture was shaken for 14 hours. The aluminum hydroxide was filtered off, washed and extracted with methanol in a Soxhlet apparatus. The combined extracts were evaporated in vacuum. To the residue was added 100 ml of water and the oily methyl ester of ε-[5-(1-acetylaminoethyl)-2-thienyl]-caproic acid liberated, which had an alkaline reaction to litmus, was extracted with ether and the solution dried with magnesium sulfate. Removal of the ether left 7.9 g of a pale yellow oil. To the latter was added 2.35 g of sodium hydroxide in 30 ml of water. The mixture was boiled for three hours, when the oil dissolved completely. The solution was cooled to 50° and filtered and 10 ml of acetic anhydride gradually added. The mixture was stirred for one hour. The separated oil was dissolved by the addition of sodium hydroxide and the solution acidified with hydrochloric acid. The oil thus liberated partially crystallized on standing in a refrigerator. The weight of the substance was 7.2 g (the yield of the impure acetylamino acid was 69%, calculated on the oxime).

11-Acetylaminolauric acid. To a solution of 7.2 g of oily ε-[5-(1-acetylaminoethyl)-2-thienyl]-caproic acid in a mixture of 300 ml of water and 50 ml of concentrated ammonia solution, heated to 65°, was added 50 g of Raney nickel with vigorous stirring. The mixture was stirred at 65-70° until there was no reaction for sulfur (sodium nitroprusside test). The nickel was filtered off and washed several times with warm, dilute ammonia solution. The combined filtrates were evaporated to dryness in vacuum on a water bath. The residue was dissolved in 50 ml of 5% sodium hydroxide and the solution filtered free from nickel hydroxide. Acidification of the filtrate with hydrochloric acid liberated an oil, which rapidly crystallized. The weight of dry material was 2.85 g (43.5%); the m.p. was 88-91°. After recrystallization from dilute methanol, the acetylamino acid had m.p. 94-95°.

Found %: C 65.47, 65.28; H 10.42, 10.30; N 5.70, 5.71. $C_{14}H_{27}O_3N$. Calculated %: C 65.33; H 10.58; N 5.44.

The reduction of the esters of the oximino acids with amalgamated aluminum is not obligatory in the cases described above and the corresponding aliphatic amino acids may be obtained by direct hydrogenolysis of the oximino acids.

10-Aminoundecanoic acid (V, R = H, R' = CH_3, n = 3). To a solution of 5.0 g of unpurified oximino acid (III, R = H, R' = CH_3, n = 3) in 200 ml of water and 50 ml of concentrated ammonia, heated to 65°, was added 42 g of Raney nickel with vigorous stirring. Stirring at 65-70° was continued until there was a negative reaction

TABLE 3

Amino acids and their derivatives	M.p.	Yield (%)	Empirical formula	%C		%H		%N		%Cl	
				found	calc.	found	calc.	found	calc.	found	calc.
10-Aminoundecanoic acid*	185—186°	40	$C_{11}H_{23}O_2N$	65.61, 65.86	65.63	11.32, 11.35	11.51	7.27, 7.30	6.96	—	—
Hydrochloride	152—153	—	$C_{11}H_{24}O_2NCl$	55.47, 55.53	55.56	9.97, 9.97	10.17	—	—	14.72, 14.58	14.91
Acetyl derivative	94—95	—	$C_{13}H_{25}O_3N$	63.79, 63.95	64.16	10.00, 10.02	10.35	—	—	—	—
Benzenesulfonyl derivative**	126—127	—	—	—	—	—	—	—	—	—	—
11-Aminolauric acid	199—200	49	$C_{12}H_{25}O_2N$	66.63, 66.59	66.93	11.41, 11.57	11.70	6.46, 6.71	6.51	—	—
Hydrochloride	125.5—126.5	—	$C_{12}H_{26}O_2NCl$	56.97, 56.88	57.24	10.20, 10.24	10.41	—	—	13.98, 13.88	14.08
9-Aminoundecanoic acid	166—168	50	$C_{11}H_{23}O_2N$	65.23, 65.17	65.63	11.41, 11.28	11.51	7.09, 6.92	6.96	—	—
Hydrochloride	131—132	—	$C_{11}H_{24}O_2NCl$	55.40, 55.25	55.56	10.01, 9.98	10.17	—	—	14.85, 14.69	14.91
11-Aminotridecanoic acid	162.5—164	24	$C_{13}H_{27}O_2N$	67.70, 67.82	68.07	11.64, 11.50	11.87	6.39, 6.43	6.11	—	—
Hydrochloride	139—140	—	$C_{13}H_{28}O_2NCl$	58.66, 58.67	58.73	10.74, 10.63	10.62	—	—	13.28, 13.25	13.34

*Literature data [1, 2]: m.p. 186-187°; 186°.

**Literature data [2]: m.p. 126-127°.

for sulfur (about nine hours). The nickel was filtered off and washed with dilute ammonia solution. The combined filtrates were evaporated to dryness in vacuum. The amino acid, containing a small amount of aluminum hydroxide, was purified by recrystallization from water.

Similar hydrogenolysis of appropriate oximino acids of general formula (III) yielded 11-aminolauric (V, R = H, R' = CH_3, n = 4), 9-aminoundecanoic (V, R = H, R' = C_2H_5, n = 3) and 11-aminotridecanoic (V, R = H, R' = C_2H_5, n = 5) acids. The constants of the amino acids and their derivatives are presented in Table 3 (the yields are given for the unpurified substances and the melting points of the amino acids for materials recrystallized from water).

The hydrochlorides were obtained by heating the amino acids with dilute (1:1) hydrochloric acid and purified by recrystallization from a mixture of anhydrous isopropyl alcohol and acetone.

SUMMARY

1. The action of acetyl and propionyl chlorides on the esters of ω-(2-thienyl)-alkanoic acids in the presence of stannic chloride yielded the esters of δ-(5-acetyl-2-thienyl)-valeric, ϵ-(5-acetyl-2-thienyl)-caproic, γ-(5-propionyl-2-thienyl)-butyric and ϵ-(5-propionyl-2-thienyl)-caproic acids; the corresponding keto acids were prepared by hydrolysis of these esters.

2. Hydrogenolysis of the oximes, prepared from the keto acids of the thiophene series listed, by means of Raney nickel yielded 10-aminoundecanoic, 11-aminolauric, 9-aminoundecanoic and 11-aminotridecanoic acids.

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SYNTHESIS AND CONVERSIONS OF SOME DI-(2-THIENYL)METHANE DERIVATIVES

V. THE ACTION OF n-BUTYLLITHIUM ON 5-METHYL- AND 5,5'-DIMETHYL-2,2'-DITHIENYLMETHANE

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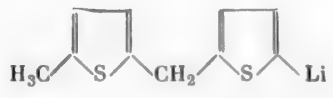
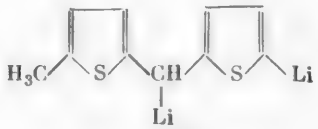
We previously showed [1] that in the action of n-butyllithium in ether solution on di-(2-thienyl)methane (I), the α-hydrogen atoms of the latter are readily replaced with the formation of mono- and dilithium derivatives. Meanwhile, the analog of (I), diphenylmethane, gives diphenylmethyllithium with n-butyllithium [2]. Similar substitution products (in the methylene group) are formed in the reaction of diphenylmethane, and also di-(2-thienyl)methane, with amides of alkali metals in liquid ammonia [3, 4]. Such a difference in aromatic systems of similar nature in their behavior toward lithiumalkyls and, on the other hand, the similarity of their reactions with amides of alkali metals may be explained by a difference in the character of the metallating action of the agents of the first and second types.

A mechanism for the metallation of compounds containing a heteroatom by means of lithiumalkyls was put forward by Roberts et al. [5] and expounded in more detail by Gronowitz [6] for certain substituted thiophenes. He postulated an initial coordination between a lithium cation and the sulfur atom, which facilitates polarization of the neighboring C–H bonds. After this initial stage, the ortho-hydrogen atom of the thiophene ring is removed as a result of nucleophilic attack by the carbanion of the metallating agent. In contrast to this, the action of lithiumorganic compounds or metal amides on diphenylmethane and di-(2-thienyl)methane may be considered as an acid-base interaction, without the intermediate formation of a complex [7].

In the light of the data presented, it seemed interesting to study the behavior of α-mono- and, in particular, α,α'-dialkylsubstituted dithienylmethanes toward n-butyllithium. In accordance with the ideas presented, one might assume that, in these cases, the rate of metallation in the nucleus by lithiumalkyls should be reduced sharply, since the α-hydrogen atom has been replaced and, in addition, the nucleus is deactivated with respect to nucleophilic substitution by alkyl groups. Due to this, from 5,5'-dimethyl-2,2'-dithienylmethane (II) one should obtain predominantly or exclusively the product of metallation in the methylene group and in the case of the monomethylsubstituted derivative (III), one might expect the formation of two metalloorganic compounds, (IV) and (V).



(IV)

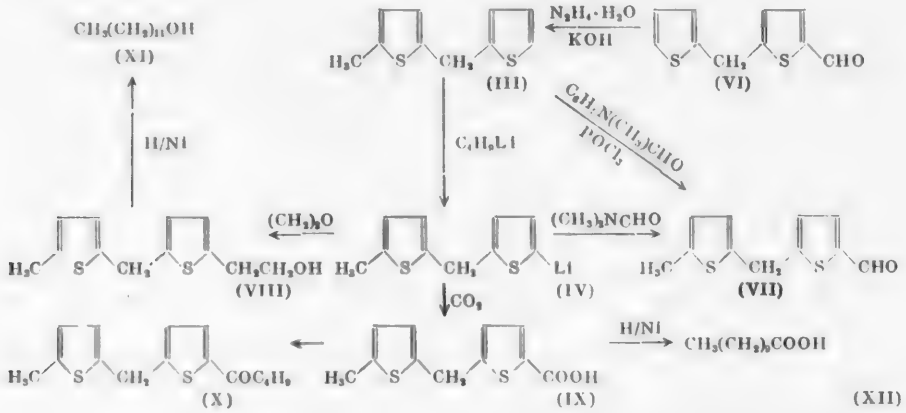


(V)

As will be seen from what is presented below, these ideas are only partially justified by experiment.

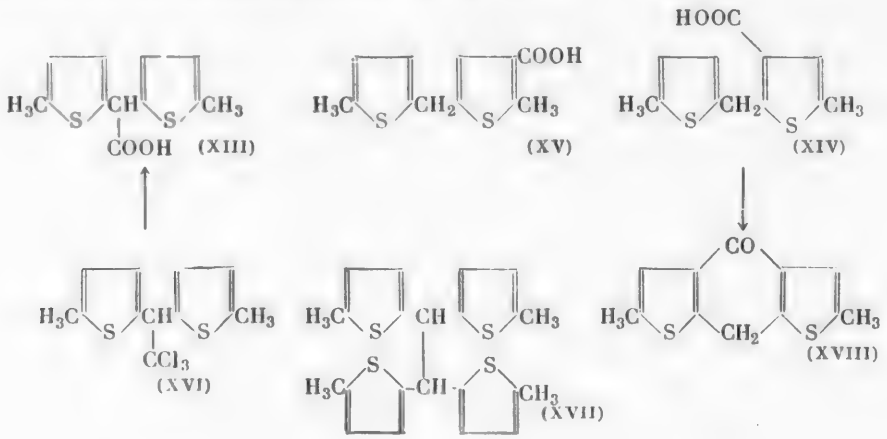
We prepared the 5-methyl-2,2'-dithienylmethane (III) required for the investigation by a Kizhner reduction of 5-(2-thienyl)-2-thiophenealdehyde [8] (VI). Compound (III) was previously described by Gol'dfarb and Konstantinov [9]. Metallation of 5-methyl-2,2'-dithienylmethane with an equivalent amount of n-butyllithium and

subsequent treatment with N,N-dimethylformamide, ethylene oxide or carbon dioxide formed an aldehyde, which was identical with 5'-methyl-2,2'-dithienylmethyl-5-aldehyde (VII) synthesized previously [9], an alcohol (VIII) and an acid (IX), respectively.* Reductive desulfurization of the latter with Raney nickel gave n-dodecyl alcohol (XI) and undecanoic acid (XII). By these data it was established that the structures of the compounds obtained in the reactions with ethylene oxide and carbon dioxide corresponded to 5-(β-hydroxyethyl)-5'-methyl-2,2'-dithienylmethane (VIII) and 5'-methyl-2,2'-dithienylmethane-5-carboxylic acid (IX) and also that the original lithiumorganic compound had the structure (IV). If we consider that, in the experiment with ethylene oxide, the total weight of methyldithienylmethane recovered and consumed in the formation of alcohol (VIII) was more than 80% of the starting amount, then we can accept that reaction of the latter with n-butyllithium mainly forms derivative (IV).



5,5'-Dimethyl-2,2'-dithienylmethane (II), obtained in 71% yield by the method of Gol'dfarb and Danyushevskii [8], metallated badly under the same conditions (−5°); this was indicated by the amount of butane liberated and the yield of acid in the carboxylation, when 77% of original (II) was recovered unchanged. Changing the metallation temperature (+35°) did not give a positive result. Here we should note that the reduced lability of the methylene hydrogen atoms in 5,5'-dimethyl-2,2'-dithienylmethane may be attributed to the effect of the methyl groups, whose inductive effect opposes the effect of σ,π-conjugation, with which this lability is connected. However, in comparing the action of n-butyllithium on diphenylmethane and phenyl-p-tolylmethane, Gilman observed an opposite effect and found an increase in yield of lithium substituted derivative in going from the first to the second compound [2].

The acid with m.p. 157°, obtained from the lithiumorganic compound of (II), may be assigned structure (XIII) or, as at first seemed less probable, structure (XIV) or (XV).



*Carboxylation of the lithiumorganic compound also yielded 5-methyl-5'-valeryl-2,2'-dithienylmethane (X), which was formed by the action of n-butyllithium on the lithium salt of the acid (IX).

To elucidate this problem, we synthesized bis-(5-methyl-2-thienyl)-acetic acid (XIII) by an independent method proposed for the preparation of di-(2-thienyl)acetic acid [10]. For this purpose, 2-methylthiophene was condensed with chloral hydrate in glacial acetic acid in the presence of sulfuric acid to give 2,2-bis-(5-methyl-2-thienyl)-1,1,1-trichloroethane (XVI) [11, 12], which gave a carboxylic acid with m.p. 92° on hydrolysis. That the latter had the structure of bis-(5-methyl-2-thienyl)acetic acid was confirmed by the fact that its decarboxylation gave 5,5'-dimethyl-2,2'-dithienylmethane. In addition, in this experiment we isolated a small amount of a substance with m.p. 177°, which had the composition and molecular weight of 1,1,2,2-tetra-(5-methyl-2-thienyl)-ethane (XVII). Since the melting point (92°) of bis-(5-methyl-2-thienyl)acetic acid differed from that of the acid with m.p. 157°, the latter may be ascribed structure (XIV) or (XV). It seemed possible to make a choice between these two formulas by carrying out an internal acylation, which, in the case of acid (XIV) must lead to ketone (XVII). Unfortunately, experiments on the internal acylation did not give a definite result, largely due to the fact that we had a very small amount of the acid with m.p. 157°. Therefore, at the moment, on the basis of Gronowitz's observations [6], we can only say that structure (XIV) is the most probable one for the acid with m.p. 157°, since in nucleophilic attack, the methyl group directs lithium into the most remote position. However, this requires experimental confirmation.

EXPERIMENTAL

5-(2-Thienyl)-2-thiophenealdehyde. 60 g of phosphorus oxychloride and 53 g of freshly distilled N-methylformamide were mixed and after 30 minutes, a solution of 54 g of di-(2-thienyl)methane [8] in 150 ml of anhydrous benzene was added to the mixture with stirring at 25° over a period of 1.5 hours. After being stirred for a further two hours at 30-35°, the mixture was left overnight at room temperature and then poured with stirring into a mixture of 150 g of crushed ice and 70 ml of water. The upper layer was separated and the lower one extracted three times with 200-ml portions of ether. The ether-benzene solution was washed three times with dilute hydrochloric acid (50 ml of acid in 400 ml of water), three times with sodium bicarbonate solution, and three times with water, and dried with magnesium sulfate. The solvent was removed in vacuum and the residue yielded 20.1 g of unreacted di-(2-thienyl)methane and 35.7 g of an aldehyde, which distilled at 152-157° (3 mm) and crystallized on cooling. The yield was 91% on the di-(2-thienyl)methane which reacted. Redistillation yielded 34.8 g of aldehyde with b.p. 153-155° (3 mm). The b.p. 156-159° (3 mm) is reported in the literature for the aldehyde [8].

5-Methyl-2,2'-dithienylmethane. To a solution of 34.3 g of 5-(2-thienyl)-2-thiophenealdehyde in 280 ml of diethylene glycol was added 75 ml of 100% hydrazine hydrate and 75 g of potassium hydroxide and the 5-methyl-2,2'-dithienylmethane and excess hydrazine hydrate were steam distilled from the gently boiling mixture in a flask with a still head and a distillation condenser. The distillation was discontinued when the temperature of the mixture reached 200°. The mixture was boiled under reflux at this temperature for four hours. Water was added to the cooled solution and the rest of the substance was steam distilled. The combined distillates were extracted with ether and the ether solution washed with dilute hydrochloric acid, sodium bisulfite solution, sodium bicarbonate solution and water and dried with calcium chloride. Working up the solution in the usual way yielded 26.2 g of 5-methyl-2,2'-dithienylmethane with b.p. 109-110° (3 mm), $n^{20}D$ 1.5943. The yield was 85%. In work published previously, the following constants were given for 5-methyl-2,2'-dithienylmethane: b.p. 116-117° (6 mm), $n^{20}D$ 1.5946 [9].

5-(β-Hydroxyethyl)-5'-methyl-2,2'-dithienylmethane. To a solution of 7.8 g of 5-methyl-2,2'-dithienylmethane in 50 ml of absolute ether at −5° was added a solution of 3.2 g of butyllithium in ether and after several minutes, 2.7 g of ethylene oxide in ether. The mixture was stirred at room temperature for one hour and then treated with very dilute acid with cooling. The ether solution was separated, washed with sodium bicarbonate solution and water, and dried with magnesium sulfate. Fractionation of the reaction product yielded 1.7 g of starting material and 5.65 g of alcohol (75% yield on the dithienylmethane reacting), which distilled at 167-170° (3 mm). After redistillation, the alcohol had the constants:

B.p. 156-157° (2 mm), $n^{20}D$ 1.5939, d^{20}_4 1.192, MR_D 67.86; calc. 67.39.

Found %: C 60.21, 60.45; H 6.16, 6.17; S 26.72, 26.65. $C_{12}H_{14}OS_2$. Calculated %: C 60.46; H 5.92; S 26.90.

The phenylurethan of 5-(β-hydroxyethyl)-5'-methyl-2,2'-dithienylmethane melted at 68-69° after recrystallization from 80% alcohol.

Found %: C 63.86, 63.89; H 5.36, 5.54; S 18.23, 18.05. $C_{19}H_{19}O_2NS_2$. Calculated %: C 63.85; H 5.36; S 17.94.

5'-Methyl-2,2'-dithienylmethane-5-aldehyde. To a solution of lithium substituted 5-methyl-2,2'-dithienylmethane in ether, prepared by the usual method from 4.9 g of 5-methyl-2,2'-dithienylmethane, was added a solution of 2.5 g of N,N-dimethylformamide in 5 ml of ether at 0°. A rise in temperature was observed and a precipitate formed. The mixture was stirred at 0° for one hour and then treated with dilute hydrochloric acid. The ether layer was separated, washed with dilute hydrochloric acid, sodium bicarbonate solution and water, and dried with magnesium sulfate. On further treatment, the solution yielded 1.9 g of starting material and 2.1 g of an aldehyde as a thick, yellow oil, which distilled at 152-156° (3 mm), and had $n^{20}D$ 1.6200. According to data in [9], the compound has the following constants: b.p. 156-158° (3 mm), $n^{20}D$ 1.6218. An aqueous alcohol solution of 0.1 g of the aldehyde, 0.5 g of hydroxylamine and 0.42 g of KOH was boiled for 1.5 hours. The cooled solution was acidified with hydrochloric acid and diluted with water. After recrystallization from 80% alcohol and a mixture of benzene and heptane, the precipitated oxime melted at 119-120°, which agrees with previously published data [9]. The melting point of a mixture of our oxime and the oxime obtained by one of us and Konstantinov was not depressed.

Found %: N 5.90, 5.99. $C_{11}H_{11}ONS_2$. Calculated %: N 5.90.

If the oxime was precipitated from the alkaline solution with water, then after two recrystallizations from 80% alcohol it melted at 99-99.5°.

Found %: N 6.13, 6.20. $C_{11}H_{11}ONS_2$. Calculated %: N 5.90.

5'-Methyl-2,2'-dithienylmethane-5-carboxylic acid. To a solution of 7.1 g of 5-methyl-2,2'-dithienylmethane in 30 ml of dry ether at −5° was added a solution of 2 g of n-butyllithium in ether and the mixture poured onto solid carbon dioxide. After acidification with dilute hydrochloric acid, the ether layer was separated and treated with 5% NaOH solution.

From the alkaline layer we isolated 2.7 g of 5'-methyl-2,2'-dithienylmethane-5-carboxylic acid with m.p. 120-122°. The yield was 55% (calculated on the 5-methyl-2,2'-dithienylmethane which reacted). After recrystallization from 40% alcohol and heptane, the substance had m.p. 128-128.5°; the neutralization equivalent found was 235.5 and the calculated one, 238.3.

Found %: C 55.67, 55.75; H 4.23, 4.31; S 26.97, 26.95. $C_{11}H_{10}O_2S_2$. Calculated %: C 55.43; H 4.23; S 26.91.

Fractional distillation of the ether solution yielded 3.1 g of starting material and 0.6 g of 5-methyl-5'-valeryl-2,2'-dithienylmethane as a thick oil, distilling at 180-190° (6 mm). After recrystallization from acetic acid and ethyl acetate, the 2,4-dinitrophenylhydrazone of this ketone melted at 156°.

Found %: N 12.06, 11.85. $C_{21}H_{22}O_4N_4S_2$. Calculated %: N 12.19.

Undecanoic acid. 3.9 g of 5'-methyl-2,2'-dithienylmethane-5-carboxylic acid, 3.5 g of sodium carbonate, 400 ml of water and about 24 g of Raney nickel were heated together at 85-90° with stirring for two hours. The precipitate was then filtered off and washed several times with 5% sodium carbonate solution. The filtrate and wash water were combined and acidified with dilute (1:1) hydrochloric acid. The precipitated oil was extracted with ether. The ether solution was washed with water and dried with magnesium sulfate. The residue after evaporation of the ether was vacuum distilled. We isolated 2 g (69%) of an acid with b.p. 160-161° (10 mm), and m.p. 26.5-27°.

Found %: C 70.51, 70.43; H 11.78, 11.70. Neutr. equiv. 184.8. $C_{11}H_{22}O_2$. Calculated %: C 70.91; H 11.90. Neutr. equiv. 186.3.

The following constants are reported in the literature for undecanoic acid: m.p. 28.5° [13], b.p. 168° (11 mm) [14]; b.p. 164° (15 mm) [15].

Dodecyl alcohol. 3.9 g of 5-(β-hydroxyethyl)-5'-methyl-2,2'-dithienylmethane and about 18 g of Raney nickel in 150 ml of 95% ethyl alcohol were boiled with vigorous stirring for three hours. After this, a test for sulfur on the filtrate was negative. The precipitate was filtered off and extracted with alcohol in a Soxhlet apparatus for eight hours. The filtrate and the alcohol extracts were combined and the solvent removed using a flask fitted

with a large pear fractionating column and a full reflux head. The residue was dissolved in ether and dried with magnesium sulfate. Treatment of the ether solution in the usual way yielded 2.2 g of dodecyl alcohol with b.p. 132° (9 mm) and m.p. 21°.

Found %: C 76.90, 76.90; H 13.84, 13.83. $C_{12}H_{26}O$. Calculated %: C 77.35; H 14.07.

The phenylurethan of dodecyl alcohol melted at 76.5-77° after recrystallization from 80% alcohol and heptane.

Found %: C 74.35, 74.31; H 9.96, 10.02. $C_{19}H_{31}O_2N$. Calculated %: C 74.71; H 10.23.

Literature data for dodecyl alcohol: m.p. 22.6° [16], b.p. 129-131° (10 mm) [17], b.p. 130.3-130.4° (7 mm) [18]; phenylurethan, m.p. 78° [19].

5,5'-Dimethyl-2,2'-dithienylmethane-(3 or 4)-carboxylic acid. To a solution of 22 g of 5,5'-dimethyl-2,2'-dithienylmethane in 50 ml of dry ether at −5° was added a solution of 7.7 g of n-butyllithium in ether. After being stirred for 15 minutes, the mixture was poured onto a mixture of dry ice and ether. When the carbon dioxide had evaporated, the mixture was treated with very dilute acid and the ether layer separated and extracted several times with 5% aqueous NaOH solution. The alkaline solution was acidified with dilute hydrochloric acid and the precipitated acid extracted with ether. The acid remaining after evaporation of the ether was pressed out on a porous plate and it weighed 3.1 g. The yield of crude acid was 51% (on the 5,5'-dimethyl-2,2'-dithienylmethane which reacted). After two recrystallizations from 50% alcohol and heptane, the acid melted at 157°.

Found %: C 57.07, 57.04; H 4.81, 4.78; S 25.40, 25.32. $C_{12}H_{12}O_2S_2$. Calculated %: C 57.11; H 4.79; S 25.41.

After treatment with aqueous alkali, the ether solution was washed with water and dried with calcium chloride. From it we isolated 17 g (77.2%) of unreacted 5,5'-dimethyl-2,2'-dithienylmethane.

2,2-Bis-(5-methyl-2-thienyl)-1,1,1-trichloroethane. To a solution of 15.3 g of chloral hydrate in 25 ml of glacial acetic acid was added 18.1 g of 2-methylthiophene and at 10-13°, 44.5 g of concentrated sulfuric acid was added over a period of 2.5 hours. The mixture was then stirred at 20° for four hours.* The thick mass formed was poured into ice water, the solid precipitate dissolved in ether, the ether solution washed with sodium bicarbonate solution and dried with calcium chloride, the ether removed and the solid residue washed with alcohol; we obtained 22.5 g (75%) of a substance, which melted at 63-65°. After recrystallization from alcohol, the substance melted at 68.5-69°. The m.p. 70-71° is reported in the literature [11].

Bis-(5-methyl-2-thienyl)acetic acid. To a mixture of 14.7 g of 2,2-bis-(5-methyl-2-thienyl)-1,1,1-trichloroethane and 60 ml of diethylene glycol was added a solution of 18.9 g of KOH in 13 ml of water. The mixture was stirred and boiled for 3.5 hours at 135° and then cooled and poured into ice water. The aqueous solution was filtered free from a dark tar and heated with activated charcoal for 15 minutes on a boiling water bath. The filtrate was cooled to 0° and acidified with 50% hydrochloric acid. The precipitated acid was filtered off and washed with water. We obtained 6.4 g (56%) of product with m.p. 90-91°. After recrystallization from 50% alcohol and from water, the acid melted at 92°.

Found %: C 57.39, 57.60; H 4.95, 5.00; S 25.40, 25.66. $C_{12}H_{12}O_2S_2$. Calculated %: C 57.11; H 4.79; S 25.41.

Decarboxylation of bis-(5-methyl-2-thienyl)acetic acid. A mixture of 5.3 g of acid, 1.5 g of powdered copper and 25 ml of quinoline was slowly heated to 190°. The evolution of gas began at 160°. When the evolution of gas ceased, the reaction mixture was cooled, diluted with ether, the copper powder filtered off and the ether solution treated with ice and 50 ml of dilute hydrochloric acid (1:1). The ether layer was separated, washed with dilute hydrochloric acid, $NaHCO_3$ solution and water, and dried with magnesium sulfate. Removal of the ether left 2.8 g of a solid substance, which was washed with alcohol and recrystallized from alcohol. Part of the substance dissolved in alcohol with difficulty. Recrystallization from ethyl acetate yielded 0.25 g of a substance with m.p. 177°.

*Truitt et al. [12] recommend stirring for 24 hours. However, we noticed that with such prolonged stirring, a more impure product was obtained. Using the method of Feeman et al. [20], we were unable to obtain 2,2-bis-(5-methyl-2-thienyl)-1,1,1-trichloroethane in a crystalline state.

Found %: C 63.68, 63.52; H 5.08, 5.22; S 30.30, 30.13. M 425.3. $C_{22}H_{22}S_4$. Calculated %: C 63.72; H 5.35; S 30.93. M 414.66.

From the composition and molecular weight, this substance may be considered as 1,1,2,2-tetra-(5-methyl-2-thienyl)ethane.

The substance, which was more soluble in hot alcohol (1.8 g), melted at 39°; it did not depress the melting point of 5,5'-dimethyl-2,2'-dithienylmethane.

SUMMARY

1. An investigation was made of the interaction of n-butyllithium with 5-methyl-2,2'-dithienylmethane. It was shown that under the conditions chosen by the authors, this compound gives a product of monometallation in the thiophene ring.

2. In experiments on the metallation of 5,5'-dimethyl-2,2'-dithienylmethane and the subsequent action of carbon dioxide, it was possible to isolate only small amounts of an acid of undetermined structure which, however, differed from bis-(5-methyl-2-thienyl)acetic acid.

3. The action of ethylene oxide or carbon dioxide on the lithium derivative of 5-methyl-2,2'-dithienylmethane yielded an alcohol and an acid, respectively, which were converted to dodecyl alcohol and undecanoic acid by reductive desulfurization.

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REACTIONS OF ORGANOMONOHYDROXYSILANES WITH ISOCYANATES (SYNTHESIS OF SILICOORGANIC URETHANS)

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From the literature it is known that organic alcohols react with isocyanates without the formation of side products. The reaction, as Wurtz first showed [1], is accompanied by migration of the hydrogen atom of the alcohol hydroxyl group to the nitrogen atom of the isocyanate group.

We established [2] that trialkylhydroxysilanes react with diisocyanates similarly to organic alcohols by the scheme

$$R\langle^{NCO}_{NCO} + 2HOSiR_3 \rightarrow R\langle^{NHCOOSiR_3}_{NHCOOSiR_3}.$$

We called the compounds obtained silicoorganic urethans. They were white, crystalline substances, which dissolved in benzene, toluene and ether.

The starting organomonohydroxysilanes should not contain water, as it causes the formation of polyureas.

$$OCNRNCO + H_2O \rightarrow OCNRNH_2 + CO_2$$
$$OCNRNH_2 + OCNRNCO \rightarrow OCNRNHCOHNRNCO, \text{ etc.}$$

The silicoorganic urethans were very sensitive to hydrolysis. The hydrolysis proceeded readily under the action of water in the absence of catalysts. To prove the structure of the urethans, a study was made of the hydrolytic cleavage reactions of the latter. From the study of the hydrolysis products, it was established that the cleavage of the silicoorganic urethans proceeds by the scheme

$$R\langle^{NHCOOSiR_3}_{NHCOOSiR_3} + 2H_2O \rightarrow R\langle^{NH_2}_{NH_2} + 2CO_2 + 2HOSiR_3.$$

EXPERIMENTAL

Synthesis of toluylene-2,4-bis-carboaminotriethylsilane. A mixture of 43.5 g of freshly distilled meta-toluylenediisocyanate [b.p. 127° (16 mm), $n^{20}D$ 1.5665] and 132 g of triethylhydroxysilane [b.p. 69.5° (18 mm), $n^{20}D$ 1.4331; containing 12.8% of OH groups] was placed in a round-bottomed flask connected to a reflux condenser, closed with a calcium chloride tube. The contents of the flask were heated with periodic mixing on a paraffin bath at 80-85° for one hour. The liberation of gaseous products was not detected during the heating, indicating that no traces of water were present in the triethylhydroxysilane. After being cooled to room temperature, the contents of the flask were transferred to a filter, washed several times with benzine, dried in air, and recrystallized from hot, anhydrous toluene. We obtained 39.4 g (36%) of a white powder with m.p. 152-153°.

Found %: C 57.50, 57.46; H 8.66, 8.58; Si 13.10, 13.01; N 6.54, 6.64. M 449. $C_{21}H_{38}O_4N_2Si_2$. Calculated %: C 57.53; H 8.67; Si 12.78; N 6.39. M 438.

Hydrolysis of toluylene-2,4-bis-carboaminotriethylsilane. The toluylene-2,4-bis-carboaminotriethylsilane was hydrolyzed in a two-necked flask, fitted with a reflux condenser connected to a trap with sulfuric acid, a U-shaped calcium chloride tube for drying the carbon dioxide, two successive potash bulbs with concentrated KOH solution to trap carbon dioxide and a control calcium chloride tube. The second neck of the flask was connected to a tank with nitrogen. Into the flask was placed 4.0078 g of toluylene-2,4-bis-carboaminotriethylsilane and 50 ml of water. The contents of the flask were boiled for four hours, while a constant, gentle stream of nitrogen was passed. As a result of the hydrolysis two layers formed in the flask, an upper one (triethylhydroxysilane) and a lower one containing meta-toluylenediamine.

The flask was cooled to room temperature and the upper layer extracted three times with petroleum ether in 25-30 ml portions. After each extraction, the lower layer was run into the reaction flask from the separating funnel. The petroleum ether was distilled from the ether extract under water-pump vacuum. We isolated 2.349 g (97.24%) of triethylhydroxysilane with b.p. 162-163°. According to literature data [3], the boiling point of triethylhydroxysilane is 153-154°.

Found %: C 54.43, 54.68; H 12.14, 12.15; Si 21.46, 21.74. $C_6H_{16}SiO$. Calculated %: C 54.50; H 12.12; Si 21.21.

The higher boiling point of the triethylhydroxysilane in comparison with literature data is evidently caused by small traces of hexaethyldisiloxane.

The contents of the reaction flask were transferred to a Wurtz flask. The separating funnel and the reaction flask were carefully washed with ethyl alcohol and the wash alcohol also transferred to the Wurtz flask. The ethyl alcohol and water were distilled off at first under normal pressure and then in vacuum. The weight of the residue of meta-toluylenediamine with m.p. 97-98°, after removal of the alcohol and water, was 1.03 g (91.9%). Recrystallization from alcohol yielded 0.78 g (70%) of meta-toluylenediamine with m.p. 98-99°.

Found %: C 69.08, 69.13; H 7.95, 7.95; N 22.48, 22.41. $C_7H_{10}N_2$. Calculated %: C 68.85; H 8.19; N 22.95.

The amount of CO_2 liberated was determined from the increase in total weight of the potash bulbs and the control tube, which equaled 0.7952 g (98.75%).

Synthesis of toluylene-2,4-bis-carboaminodiethylpropylsilane. A mixture of 43.5 g of freshly distilled meta-toluyleneisocyanate (m.p. 21°, d^{20}_4 1.2385, $n^{20}D$ 1.5663) and 73 g of diethylpropylhydroxysilane [b.p. 171-172° (747 mm), $n^{20}D$ 1.4365; containing 11.7% of OH groups] were placed in a round-bottomed flask connected to a condenser, closed with a calcium chloride tube. With periodic mixing, the contents of the flask were heated on a paraffin bath at 80-85° for one hour. The evolution of gaseous products during the heating was not observed, indicating that traces of water were absent from the diethylpropylhydroxysilane. After being cooled to room temperature, the contents of the flask were transferred to a filter, washed several times with benzine, dried in air, and recrystallized from hot, anhydrous toluene. We obtained 38.44 g (33%) of a white powder with m.p. 140-141°.

Found %: C 58.97, 58.95; H 9.08, 9.12; N 6.2, 6.3; Si 12.02, 11.70. M 449.8. $C_{23}H_{42}O_4N_2Si_2$. Calculated %: C 59.22; H 9.01; N 6.00; Si 12.01. M 466.

Hydrolysis of toluylene-2,4-bis-carboaminodiethylpropylsilane. The experiment was similar to the one described above. In the reaction was used 4 g of toluylene-2,4-bis-carboaminodiethylpropylsilane and 50 ml of water. The total increase in weight of the potash bulbs and the control calcium chloride tube was 0.7425 g (98.3%). As in the hydrolysis of toluylene-2,4-bis-carboaminotriethylsilane, two layers were formed in the reaction flask, the upper one oily (diethylpropylhydroxysilane) and the lower containing meta-toluylenediamine.

Synthesis of toluylene-2,4-bis-carboaminodiethylbutylsilane. A mixture of 43.5 g of freshly distilled meta-toluylenediisocyanate (m.p. 21°, d^{20}_4 1.2385, $n^{20}D$ 1.5663) and 80 g of diethylbutylhydroxysilane [b.p. 190° (744 mm), $n^{20}D$ 1.4390; containing 10.6% of OH groups] was placed in a round-bottomed flask connected to a condenser, fitted with a calcium chloride tube. With periodic mixing, the contents of the flask were heated on a paraffin bath at 80-85° for one hour. The evolution of gaseous products during heating was not observed, indicating that traces of water were not present in the diethylbutylhydroxysilane. After cooling to room temperature, the contents of the flask were transferred to a filter and washed several times with benzine, then dried in air, and recrystallized from hot, anhydrous toluene. We obtained 37.05 g (30%) of a white powder with m.p. 104-106°.

Found %: C 60.66, 60.52; H 9.42, 9.47; N 6.05, 6.13; Si 11.3. M 479. $C_{25}H_{46}O_4N_2Si_2$. Calculated %: C 60.72; H 9.31; N 5.66; Si 11.33. M 494.

SUMMARY

1. Three silicoorganic urethans which are not described in the literature were synthesized and their structures established.

2. It was found that silicoorganic urethans are readily hydrolyzed by the action of water in the absence of catalysts with the formation of a diamine, a trialkylhydroxysilane and carbon dioxide

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INVESTIGATIONS IN THE FIELD OF ALKOXYSILANES

XIII. THE REACTION OF SILOXANES WITH ALKOXYSILANES. A NEW METHOD OF SYNTHESIZING ALKOXYSILANES AND SILOXANES*

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We previously showed [2] that it was possible to prepare organoalkoxysilanes by cleavage of organosiloxanes with alcohols in the presence of alkaline catalysts by the general scheme

$$1/m(R_nSiO_{2-0.5n})_m + (4-n)R'OH \xrightarrow[-0.5(4-n)H_2O]{R'O^-} R_nSi(OR')_{4-n},$$

where $n = 1-3$, R represents similar or different hydrocarbon radicals and the degree of polymerization, m, may be varied over a wide range.

This synthesis was accomplished under conditions which ensured that the water formed was removed from the reaction sphere either by continuous azeotropic distillation or by dehydrating agents. In particular, for the latter we used tetraalkoxysilanes, which are readily hydrolyzed by water in an alcoholic alkaline medium (cf. [3]).

$$Si(OR)_4 + 4H_2O \rightarrow 4ROH + Si(OH)_4 \rightarrow SiO_2 + 2H_2O$$

Thus, for example, the formation of dimethyldiethoxysilane from polydimethylsiloxane and ethyl alcohol in the presence of tetraethoxysilane may be represented by the following equations.

$$[(CH_3)_2SiO]_n + 2nC_2H_5OH \xrightleftharpoons{KOH} n(CH_3)_2Si(OC_2H_5)_2 + nH_2O \quad (n \geqslant 3)$$

$$nH_2O + 0.5nSi(OC_2H_5)_4 \xrightarrow{KOH} 0.5(SiO_2)_n + 2nC_2H_5OH$$

Summarizing these equations shows that the reaction proceeds by the scheme

$$2[(CH_3)_2SiO]_n + nSi(OC_2H_5)_4 \xrightarrow{KOH} 2n(CH_3)_2Si(OC_2H_5)_2 + (SiO_2)_n.$$

Consequently, the alcohol hardly participates in the reaction and the formation of dimethyldiethoxysilane proceeds by the interaction of polydimethylsiloxane with tetraethoxysilane.

Experiments completely confirmed this hypothesis. We showed that simple distillation of a mixture of a linear, branched or cyclic organosiloxane with a tetraalkoxysilane (or an organoalkoxysilane) in the presence of an alkaline catalyst (for example, KOH) gave an excellent yield of the corresponding organoalkoxysilane. Thus, we found a new, simple and convenient method of preparing organoalkoxysilanes, based on the cleavage of organosiloxanes by alkoxysilanes. In the case of $Si(OR)_4$, the reaction may be represented by the following general scheme:

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$$4/m(R_nSiO_{2-0.5n})_m + (4-n)Si(OR')_4 \xrightarrow{R'O^-} 4R_nSi(OR')_{4-n} + (4-n)SiO_2,$$

where n = 2-3 and m may be varied over a wide range.

By this method, we prepared the series of dialkyldialkoxy- and trialkylalkoxysilanes presented in Table 1. We should note that the reaction of tetraalkoxysilanes with hexaalkyldisiloxanes, where the electrophilic nature of the silicon atoms is weaker than in other organosiloxanes, proceeded very much more slowly and the yields of the trialkylalkoxysilanes could have been better (below 50%). However, in the presence of other organosiloxanes, containing the grouping R_3SiO [for example, $(R_3SiO)_4Si$ or $(R_3SiO)_3SiR''$], the yields of trialkylalkoxysilanes reached 75-85%. In the case of $(R_3SiO)_3SiR''$, alkyltrialkoxysilanes were formed together with trialkylalkoxysilanes and linear polyalkylsiloxanes formed simultaneously the corresponding dialkyldialkoxy- and trialkylalkoxysilanes.

$$2R''Si(OSiR_3)_3 + 3Si(OR')_4 \xrightarrow{KOH} 2R''Si(OR')_3 + 6R_3SiOR' + 3SiO_2$$

$$R_3Si(OSiR_2)_nOSiR_3 + (n+0.5)Si(OR')_4 \xrightarrow{KOH} 2R_3SiOR' + nR_2Si(OR')_2 + (n+0.5)SiO_2$$

Thus, for example, the reaction of methyltris(trimethylsiloxy)silane with tetramethoxysilane formed trimethylmethoxysilane and methyltrimethoxysilane in yields of 36 and 48%, respectively, while the interaction of octamethyltrisiloxane with tetraethoxysilane gave trimethylethoxysilane and dimethyldiethoxysilane (50 and 80%, respectively).

Instead of tetraalkoxysilanes, one may introduce into the reaction the organoalkoxysilanes, $R_nSi(OR')_{4-n}$ (n = 1-3), which are converted into the corresponding mono- or polymolecular organosiloxanes. Thus, for example, the reaction of octamethylcyclotetrasiloxane with trimethyl-n-amoxysilane proceeded by the scheme (in this case R, R'' = CH_3 and R' = n-C_5H_{11}):

$$1/m(R_2SiO)_m + 2R''_3SiOR' \xrightarrow{KOH} R_2Si(OR')_2 + R''_3SiOSiR''_3,$$

whereby the yield of hexamethyldisiloxane and dimethyldiamoxysilane were 57% and 56%, respectively.

A mixture of polyethoxysiloxanes was formed in the reaction of polydimethylsiloxane with excess tetraethoxysilane.

$$(n-1)/m(R_2SiO)_m + nSi(OR')_4 \xrightarrow{R'O^-} (n-1)R_2Si(OR')_2 + (R'O)_3Si[OSi(OR')_2]_{n-1}OR'$$

From the mixture we isolated individual compounds with n = 2-3 (compounds with n > 3, which were formed, were not identified).

The reaction of polydimethylsiloxane with excess methyltri-n-butylsilane proceeded similarly and gave polysiloxanes of the type (R'O)RSi[OSi(OR')R]$_n$OR'. We should note that, in both cases, the reaction mixture was filtered and acidified with metaphosphoric acid, after distillation of the dialkyldialkoxysilane, to prevent disproportionation of the alkoxysiloxanes formed.

The examples presented above indicate that the reaction of alkoxysilanes with siloxanes is also applicable as a method of preparing siloxanes. The processes thus occurring may be compared in a purely formal way with a hydrolysis of alkoxysilanes in which the role of water is played by an organosiloxane.

Together with individual low and high-molecular organosiloxanes and various mixtures of them, it is also possible to use as starting materials for the synthesis of organoalkoxysilanes and siloxanes, polyorganosiloxanes – incompletely condensed hydrolysis products of organohalosilanes.

The reactivity of organosiloxanes in their cleavage by alkoxysilanes in the presence of alkaline catalysts falls in the series: $(R_2SiO)_{n+2} > (R_2SiO)_{n+3} > R_3Si(OSiR_2)_nOSiR_3 > R_3Si(OSiR_2)_{n-1}OSiR_3 (n \geq 1)$. Their reactivity toward bases also falls in the same order [4]. Increasing the length or the branching of the organic radicals, both in the starting siloxanes and in the alkoxysilanes hinders their reaction. Thus, for example, hexaethyldisiloxane hardly reacts with tetraisobutoxysilane, while when reacted with the latter, hexamethylcyclotrisiloxane was 70-80% converted into dimethyldiisobutoxysilane and octaethylcyclotetrasiloxane was 47% converted into diethyldiisobutoxysilane.

TABLE 1

Analysis, Physical Constants and Yields of the Siloxanes and Alkoxysilanes Obtained

Sample No.	Compound	B.p. (pressure in mm)	d^{20}_4	n^{20}_D	Si content (in %)*		Yield of unpurified product (%) and starting materials**
					found	calc.	
1	$(CH_3)_3SiOCH_3$	57.2° (760)	—	1.3679	26.80, 26.72	26.95	17–25 (1+19), *** 51 (1+21), 36 (1+22)
2	$(CH_3)_3SiOC_2H_5$	75.3 (760)	0.7573	1.3742	23.99, 23.51	23.75	78 (2+21), 65 (2+22), 45 (2+19), 50 (2+23)
3	$(CH_3)_3SiOC_3H_7$-n	98.5 (760)	0.7668	1.3838	21.44, 21.52	21.23	70 (3+21)
4	$(CH_3)_2Si(OCH_3)_2$	82.2 (760)	—	1.3705	23.07, 23.00	23.36	92 (1+13), 90 (1+14)
5	$(CH_3)_2Si(OC_2H_5)_2$	113.8 (760)	0.8401	1.3814	19.04, 19.10	18.94	86 (2+13), 84 (2+14), 81 (2+15), 78 (2+16), 80 (2+23)
6	$(CH_3)_2Si(OC_3H_7\text{-n})_2$	152 (760)	0.8417	1.3954	15.87, 16.12	15.93	81 (3+14), 78 (3+15)
7	$(CH_3)_2Si(OC_3H_7\text{-iso})_2$	133 (760)	—	1.3863	15.99, 16.08	15.93	67 (4+14)
8	$(CH_3)_2Si(OC_4H_9\text{-n})_2$	190.3 (760)	0.8431	1.4058	13.66, 13.79	13.74	60 (24), 93 (5+16)
9	$(CH_3)_2Si(OC_4H_9\text{-iso})_2$	172.0 (760)	0.8323	1.3999	13.81, 13.98	13.74	78 (6+16)
10	$(CH_3)_2Si(OC_5H_{11}\text{-n})_2$	225.5 (760)	0.8444	1.4138	12.20, 12.26	12.08	57 (14+25)
11	$(C_2H_5)_2Si(OC_4H_9\text{-iso})_2$	210 (760)	0.8455	1.4130	12.31, 12.44	12.08	47 (6+18), 50 (6+17)
12	$CH_3Si(OCH_3)_3$	103.5 (760)	—	1.3701	20.44, 20.21	20.62	48 (1+22)
13	$CH_3Si(OC_2H_5)_3$	143.5 (760)	0.8949	1.3832	15.63, 15.94	15.75	57 (2+22)
14	$Si(OCH_3)_4$	121.2 (760)	1.034	1.3688	18.51, 18.57	18.45	95 (7), 95 (3), 48 (1+22)
15	$Si(OC_2H_5)_4$	168.4 (760)	0.9335	1.3831	13.40, 13.47	13.48	84, 5 (9), 80 (10), 77 (11), 75 (12)
16	$OSi_2(OC_2H_5)_6$	100.0 (1.5)	0.9980	1.3914	16.40, 16.45	16.40	17 (2+14) ****
17	$O_2Si_3(OC_2H_5)_8$	132.5 (1)	1.030	1.3950	17.69, 17.80	17.67	13 (2+14) ****
18	$[CH_3(C_4H_9O)_2Si]_2O$	145 (1.5)	0.9196	1.4136	14.31, 14.44	14.23	16 (16+26)
19	$[CH_3(C_4H_9O)_2SiO]_2Si(OC_4H_9)CH_3$	165—170 (0.5)	—	1.4155	16.23, 15.78	15.99	10 (16+26)
20	$(CH_3)_3SiOSi(CH_3)_3$	100.4 (760)	0.7636	1.3774	34.29, 34.37	34.59	57 (14+25)

*The silicon in the volatile organoalkoxysilanes was largely determined by Smith's method [17].

**The figures in brackets refer to the numbers of the starting materials in Table 2.

***In the presence of $FeCl_3$, the yield was 36%.

****Yield of pure substance.

In our opinion, the mechanism of the cleavage reaction of organosiloxanes by alkoxysilanes is similar to the mechanism of the alkali-catalyzed rearrangement of organopolysiloxanes [4, 5]. It may be represented by the following scheme (the stars mark the silicon atom of the original alkoxysilane):

$$\equiv SiOSi\equiv + B^- \rightleftarrows \equiv SiB + \equiv SiO^-;\ (B = HO^-;\ RO^-\ \text{etc.}),$$

$$\equiv SiO^- + RO\overset{*}{S}i\equiv \rightleftarrows SiOR + \equiv \overset{*}{S}iO^-;$$

$$\equiv \overset{*}{S}iO^- + RO\overset{*}{S}i\equiv \rightleftarrows \equiv \overset{*}{S}iO\overset{*}{S}i\equiv + RO^-;$$

$$\equiv SiOSi\equiv + RO^- \rightleftarrows \equiv SiOR + \equiv SiO^-\ \text{etc.}$$

When the hydroxides of alkali metals are used as catalysts, the initiation of the reaction may proceed by another scheme*: $\equiv SiOR + KOH \rightleftarrows \equiv SiOK + ROH$, but the rest of the reaction mechanism remains the same.

Thus, the reaction considered is a base-catalyzed rearrangement of Si—O—Si and Si—O—C bonds, whose equilibrium may be displaced by removal of the most volatile component from the reaction sphere. In the particular case, this reaction may be an intramolecular rearrangement of alkoxysiloxanes, which simultaneously contain Si—O—Si and Si—O—C bonds. Thus, for example, Malatesta [6] observed the disproportionation of linear polyethoxysiloxanes in the presence of sodium or aluminum ethoxide.

$$(RO)_3Si[OSi(OR)_2]_nOSi(OR)_3 \xrightleftarrows{RO^-} Si(OR)_4 + (n+1)/m[OSi(OR)_2]_m;\ (R = C_2H_5)$$

The possibility of polymethoxysiloxanes disproportionating during their distillation has also been reported [7].

We found that the similar disproportionation of polyalkoxysiloxanes, which is also catalyzed by various alkaline reagents (KOH, etc.), may proceed more extensively and go right to the formation of SiO_2:

$$2RO[(RO)_2SiO]_nR \xrightarrow{KOH} (n+1)Si(OR)_4 + (n-1)SiO_2,$$

where $n \geq 2$. Polymethoxysiloxanes are almost quantitatively (93-95%) disproportionated and linear polyethoxysiloxanes are 75-85% disproportionated by this scheme. The cyclic polydiethoxysiloxanes are also readily disproportionated in the presence of alkali by the scheme

$$2[(RO)_2SiO]_n \xrightarrow{KOH} nSi(OR)_4 + nSiO_2.$$

This indicates that the scheme for the disproportionation of polyalkoxysiloxanes, put forward by Malatesta previously [6], is not completely correct as polydialkoxysiloxanes may disproportionate under the action of alkali right to SiO_2 or polysilicic esters with a very low content of alkoxy groups.

In the presence of alkalis, polyorganoalkoxysiloxanes also undergo the same conversions as polyalkoxysiloxanes. Thus, for example, 1,3-dibutoxytetramethyldisiloxane is 60-65% converted into dimethyldibutoxysilane when distilled over 9-10 mole % of KOH.

In conclusion, we should note that the cleavage of siloxanes by alkoxysilanes also occurs under the action of electrophilic catalysts (for example, those like ferric chloride**). Thus, in the reaction of tetramethoxysilane

*From the reaction of anhydrous KOH with R_3SiOR' or $Si(OR')_4$, together with R'OH we isolated R_3SiOK or $(R'O)_3SiOK$, respectively, which can also catalyze the reaction of alkoxysilanes with siloxanes.

**It is interesting to note that siloxanes may also be cleaved by alkoxy derivatives of certain other elements and we shall discuss this in a later communication.

with hexamethyldisiloxane in the presence of ferric chloride, the yield of trimethylmethoxysilane reached 31%, while in the presence of KOH it equaled 17-25%. However, in the presence of $FeCl_3$, octamethoxycyclotetrasiloxane hardly reacts with tetraisopropoxysilane, while when KOH is used as catalyst, dimethyldiisopropoxysilane is formed in 67% yield.

EXPERIMENTAL*

Starting materials. We previously described the synthesis and purification of the starting tetraalkoxysilanes [8, 9]. The linear polymethoxy- and polyethoxysiloxanes (cf. [6, 7, 10]) were obtained by hydrolysis of large amounts (1-1.5 kg) of $Si(OCH_3)_4$ or $Si(OC_2H_5)_4$ in the appropriate alcohol (HCl catalyst). They separated by repeated fractional distillation in vacuum on a column with a glass packing in the presence of traces of phosphoric acid.** Octaethoxycyclotetrasiloxane was prepared together with linear polyethoxysiloxanes by hydrolysis of tetraethoxysilane. 1,3-Dibutoxytetramethyldisiloxane and 1,5-dibutoxyhexamethylsiloxane were obtained by the reaction of dimethyldichlorosilane with moist n-butyl alcohol. Hexamethylcyclotrisiloxane was obtained from the liquid hydrolysis products of pure dimethyldichlorosilane [11] (destructive distillation in the presence of KOH). Fractional distillation of these also yielded octamethylcyclotetrasiloxane and decamethylcyclopentasiloxane [11]. Hexaethylcyclotrisiloxane and octaethylcyclotetrasiloxane were obtained by controlled hydrolysis of diethyldichlorosilane [12]. The linear polydimethylsiloxane was the industrial elastomer with a molecular weight of 204,700. Hexamethyldisiloxane was obtained from the azeotrope of silicon tetrachloride with trimethylchlorosilane [13] (industrial fraction from direct synthesis). Hexaethyldisiloxane was obtained by the reaction of triethylsilane with sulfuric acid in the presence of mercury sulfate [14]. Tetrakis(trimethylsiloxy)silane, methyltris(trimethylsiloxy)silane and octamethyltrisiloxane were obtained by the reaction of trimethyliodosilane with $Si(OC_2H_5)_4$, $CH_3Si(OC_2H_5)_3$ or $(CH_3)_2Si(OC_2H_5)_2$, respectively, in the absence of catalysts [9, 15]. Trimethyl-n-amoxysilane was obtained in 87% yield by the reaction of hexamethyldisiloxane with n-amyl alcohol in the presence of tetraethoxysilane [2]. Methyltri-n-butoxysilane was obtained from CH_3SiCl_3 and $n\text{-}C_4H_9OH$ in the presence of pyridine [16].

The physical constants of all the starting materials, purified by distillation on a column, are presented in Table 2.

Description of experiments. In view of the simplicity of the procedure, only the most typical experiments are described below. Data on the rest of the experiments is given in Table 1. With anhydrous potassium or sodium hydroxides used as catalysts, the formation of an amount of alcohol, equivalent to the amount of alkali taken, was observed in all experiments.

Synthesis of dimethyldiethoxysilane. 29.7 g of hexamethylcyclotrisiloxane, octamethylcyclotetrasiloxane or a mixture of liquid cyclic and linear polydimethylsiloxanes or, finally, solid, high-molecular linear polydimethylsiloxane was mixed with 83.3 g of tetraethoxysilane and 0.5-1 g of powdered KOH. When the reaction mixture was distilled, 47.5-51 g of dimethyldiethoxysilane with $n^{20}D$ 1.3813, i.e., 80-86% of theoretical, calculated on the starting polydimethylsiloxane (the yields of separate experiments are presented in Table 1), passed over at 113-114°. After distillation on a column, the dimethyldiethoxysilane had the constants presented in Table 1. Further distillation of the reaction mixture yielded 20-21 g of starting tetraethoxysilane with b.p. 163-167°; $n^{20}D$ 1.3842. A solid residue (mainly SiO_2) was left in the distillation flask.

Synthesis of dimethyldiisobutoxysilane. A mixture of 14.8 g of liquid polydimethylsiloxanes, 54.5 g of tetraisobutoxysilane and 0.5 g of KOH was distilled. This formed 38.0 g of dimethyldiisobutoxysilane with b.p. 173-181°, $n^{20}D$ 1.4000 (yield 93%) and 14.0 g of the original tetraisobutoxysilane with b.p. 241-245°, $n^{20}D$ 1.4067. After a second distillation on a column, the dimethyldiisobutoxysilane had the constants given in Table 1.

Synthesis of trimethylethoxysilane. A mixture of 19.3 g of tetrakis(trimethylsiloxy)silane, 20.8 g of tetraethoxysilane and 0.5 g of KOH was distilled slowly. 18.4 g (78%) of trimethylethoxysilane with $n^{20}D$ 1.3771 distilled over at 77-80°. Further distillation gave 10.0 g of the starting tetraethoxysilane with b.p. 163-168°, $n^{20}D$ 1.3838.

*Together with I.B. Vasil'eva.

**Otherwise the higher polymethoxysiloxanes disproportionated under the action of the alkali of the glass (and also iron, which formed $FeCl_3$ with traces of HCl), as was observed previously [7].

TABLE 2

Properties of Starting Materials

Sample No.	Formula	B.p. (pressure in mm)	d_4^{20}	n_D^{20}
1	$(CH_3O)_4Si$*	121.0°(760)	1.035	1.3689
2	$(C_2H_5O)_4Si$	168.3 (760)	0.93343	1.3830
3	$(n\text{-}C_3H_7O)_4Si$	107 (10)	0.9112	1.4012
4	$(iso\text{-}C_3H_7O)_4Si$	185.5 (760)	0.8751	1.3851
5	$(n\text{-}C_4H_9O)_4Si$	150 (10)	0.8982	1.4134
6	$(iso\text{-}C_4H_9O)_4Si$	127 (10)	0.8857	1.4068
7	$(CH_3O)_6Si_2O$	58 (1)	1.1222	1.3806
8	$(CH_3O)_8Si_3O_2$	107 (1)	1.1655	1.3869
9	$(C_2H_5O)_6Si_2O$	99 (1)	0.9979	1.3915
10	$(C_2H_5O)_8Si_3O_2$	132 (1)	1.0300	1.3950
11	$(C_2H_5O)_{10}Si_4O_3$	171 (5)	—	1.3978
12	$[(C_2H_5O)_2SiO]_4$**	156 (3)	1.0972	1.4016
13	$[(CH_3)_2SiO]_3$	134.6 (760)	M.p. 64.5°	
14	$[(CH_3)_2SiO]_4$***	175.8 (760)	0.9561	1.3968
15	$[(CH_3)_2SiO]_5$	101 (20)	0.9597	1.3982
16	$[(CH_3)_2SiO]_{2760}$	— —	*M* 204 700	
17	$[C_2H_5)_2SiO]_3$****	122.5 (10)	0.9555	1.4308
18	$[(C_2H_5)_2SiO]_4$	160 (10)	0.9636	1.4338
19	$(CH_3)_3SiOSi(CH_3)_3$	100.4 (760)	0.7636	1.3774
20	$(C_2H_5)_3SiOSi(C_2H_5)_3$	103 (10)	0.8443	1.4340
21	$[(CH_3)_2SiO]_4Si$	69 (1.5)	0.8675	1.3892
22	$[(CH_3)_2SiO]_3SiCH_3$	190 (760)	0.8500	1.3879
23	$[(CH_3)_2SiO]_2Si(CH_3)_2$	152.5 (760)	0.8200	1.3849
24	$[C_4H_9O(CH_3)_2Si]_2O$	100 (10)	—	1.405
25	$(CH_3)_3SiOC_5H_{11}$-n	145 (760)	—	1.4000
26	$CH_3Si(OC_4H_9)_3$	114 (10)	0.8771	1.4109

*M.p. 4.5°.

**M.p. 8.0°.

***M.p. 17.6°.

****M.p. 14.0°.

After distillation on a column, the trimethylethoxysilane, obtained in this way from methyltris(trimethylsiloxy)silane, had the constants presented in Table 1.

Reaction of octamethylcyclotetrasiloxane with trimethyl-n-amoxysilane. A mixture of 64.1 g of trimethyl-n-amoxysilane and 14.8 g of octamethylcyclotetrasiloxane was slowly distilled over 0.3 g of KOH. At 97-101°, 18.4 g (57%) of hexamethyldisiloxane with $n^{20}D$ 1.3795 distilled over and possessed the constants given in Table 1 after distillation over sodium. Distillation of the residue from the flask gave 26.5 g (57%) of dimethyldi-n-amoxysilane with b.p. 219-225°, $n^{20}D$ 1.4123.

Preparation of trimethylethoxysilane from hexamethyldisiloxane. Into the distillation flask of a fractionating column with an efficiency of 35 theoretical plates was placed 81.2 g of hexamethyldisiloxane, 104.2 g of tetraethoxysilane and 1.2 g of KOH. Slow distillation of the reaction mixture yielded 9.0 g of an azeotrope of trimethylethoxysilane with ethyl alcohol with b.p. 68° and 88 g of a fraction with b.p. 77-80°. Distillation of this on the same column over metallic sodium gave 48.5 g of trimethylethoxysilane with b.p. 74-75°, d^{20}_4 0.757, $n^{20}D$ 1.3742 (yield 41%, calculated on the starting hexamethyldisiloxane or 59%, calculated on that which reacted) and 24.5 g of unchanged hexamethyldisiloxane with b.p. 99-100° and $n^{20}D$ 1.3774. A further small amount of trimethylethoxysilane could be isolated from the azeotropic mixture.

Reaction of tetraethoxysilane with octamethyltrisiloxane. A mixture of 23.7 g of octamethyltrisiloxane, 31.2 g of tetraethoxysilane and 0.3 g of KOH was distilled slowly. 35.2 g of distillate was collected at 77-115°, treated with metallic sodium and distilled over it on a column. This yielded 11.8 g (50%) of trimethylethoxysilane with b.p. 75.5-75.6° (767 mm), d^{20}_4 0.757, $n^{20}D$ 1.3745 and 11.9 g (80%) of dimethyldiethoxysilane with b.p. 114.5-115.0° (768 mm), d^{20}_4 0.840, $n^{20}D$ 1.3812. Distillation of the combined high-boiling residues from the two distillations gave 10 g of starting tetraethoxysilane with b.p. 163-168°, $n^{20}D$ 1.3840.

Reaction of methyltris(trimethylsiloxy)silane with tetramethoxysilane. A mixture of 31.1 g of methyltris-(trimethylsiloxy)silane, 30.5 g of tetramethoxysilane and 0.4 g of KOH was slowly distilled; this yielded two main fractions with b.p. 55-58° (19.0 g) and 99-104° (7.0 g). Distillation of the first fraction on a column over metallic sodium gave 11.3 g (36%) of trimethylmethoxysilane with b.p. 57-58° (767 mm), $n^{20}D$ 1.3680 and 6.5 g (48%) of methyltrimethoxysilane with b.p. 102-104°, $n^{20}D$ 1.3710.

Disproportionation of hexamethoxydisiloxane and octamethoxytrisiloxane. 77.5 g of hexamethoxydisiloxane was distilled over 0.5 g of KOH. At 120-121°, 65.1 g of tetramethoxysilane with $n^{20}D$ 1.3682 (95% yield) passed over. After a second distillation on a column over metallic sodium it had the constants presented in Table 1. Similarly, on distilling 54.7 g of octamethoxytrisiloxane over 0.2 g of KOH, we obtained 43.4 g (95%) of tetramethoxysilane with b.p. 118-121°, $n^{20}D$ 1.3689. In both cases, a dry, solid white residue of SiO_2 remained in the distillation flask.

Disproportionation of octaethoxytrisiloxane and hexaethoxydisiloxane. 47.8 g of octaethoxytrisiloxane was distilled over 0.2 g of KOH. At 164-167°, 33.3 g (80%) of tetraethoxysilane with $n^{20}D$ 1.3833 distilled over. Similarly, distillation of 34.3 g of hexaethoxydisiloxane over 0.3 g of KOH yielded 26.5 g (84.5%) of tetraethoxysilane with b.p. 164-166°, $n^{20}D$ 1.3837. After a second distillation over sodium on a column, the latter had the constants presented in Table 1.

In both experiments there remained in the distillation flask a solid residue of SiO_2, which was insoluble in organic solvents, and a small amount of liquid polysilicic ester, which solidified on cooling.

Disproportionation of octaethoxycyclotetrasiloxane. 26.8 g of octaethoxycyclotetrasiloxane was distilled over 0.2 g of KOH; this gave 15.6 g (75%) of tetraethoxysilane with b.p. 165-169°, $n^{20}D$ 1.3835. The residue in the distillation flask consisted of SiO_2 and a viscous polysilicic ester, which solidified on cooling.

Preparation of polyethoxysiloxanes. A mixture of 37.1 g of octamethylcyclotetrasiloxane, 208.3 g of tetraethoxysilane and 0.6 g of KOH was distilled slowly. 75 g, i.e., the theoretical amount, of dimethyldiethoxysilane distilled over at 114-119°. The residue was filtered, 0.5 g of metaphosphoric acid added to the filtrate (160 g) and the mixture vacuum distilled. This yielded 42 g of the starting tetraethoxysilane with b.p. 57-58° (10 mm), $n^{20}D$ 1.3840. The residue (113 g) was a mixture of polyethoxysiloxanes, which distilled completely over the range 110-280° (7 mm). Fractional distillation of it on a column gave 23 g of hexaethoxydisiloxane (b.p. 100-102° at 4 mm, $n^{20}D$ 1.3912), 15 g of octaethoxytrisiloxane (b.p. 156-158° at 9 mm, $n^{20}D$ 1.3952) and also 7 g of a substance (b.p. 171° at 5 mm, $n^{20}D$ 1.3978) and 4 g of another substance (b.p. 204° at 3 mm, $n^{20}D$ 1.3997), which were not examined more closely. The infrared absorption spectra of the di- and trisiloxanes were found to be similar to the spectra of the analogous ethoxysiloxanes, obtained in the hydrolysis of tetraethoxysilane.

SUMMARY

The possibility of inter- and intramolecular rearrangement of Si—O—Si and Si—O—C bonds was demonstrated and a mechanism proposed for it. A new method was developed for the synthesis of alkoxysilanes and siloxanes by the cleavage of siloxanes by alkoxysilanes. 20 compounds of this type were prepared. A study was made of the disproportionation of linear and cyclic polyalkoxysiloxanes.

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SYNTHESIS OF THE THIOAMIDE OF 2-ETHYLISONICOTINIC ACID

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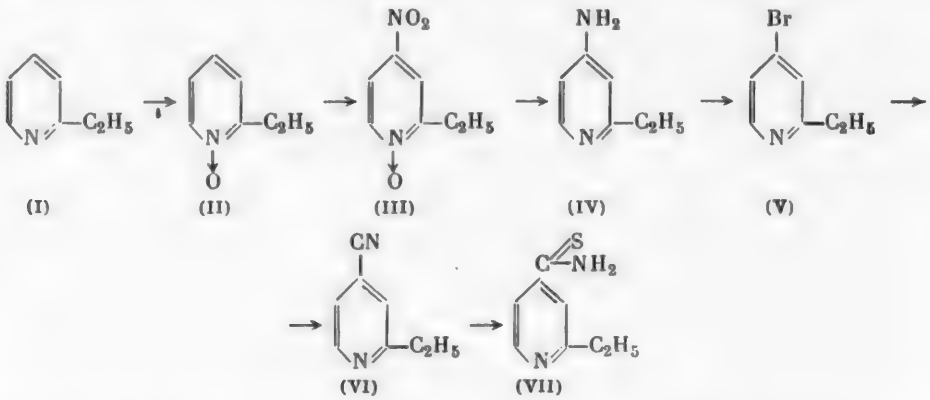
The especial value of chemotherapeutic agents, used for the treatment of tuberculosis, continuously stimulates a search for new classes of organic compounds which are suitable for this purpose. A communication [1] recently appeared on the high chemotherapeutic activity of thioamides of certain heterocyclic acids and especially the thioamide of 2-ethylisonicotinic acid, which, according to available data, is also effective against strains of Micobact. tubercul., which are resistant to other antitubercular agents. The method described in the literature for the synthesis of the thioamide of 2-ethylisonicotinic acid [2] is complicated and involves many stages so that it is inconvenient for obtaining the preparation on a large scale. In the present communication, we describe a more convenient method of synthesizing this compound. The synthesis was carried out by the following scheme:



The starting material used for the synthesis was 2-ethylpyridine (I), which was obtained by a known method [3] by hydrogenation of readily available 2-vinylpyridine. The 2-ethylpyridine was oxidized with peracetic acid in acetic acid solution to the N-oxide (II), which, without isolation in the pure state, was then nitrated with a nitrating mixture to give a yield of about 45% (on the original 2-ethylpyridine) of 2-ethyl-4-nitropyridine-N-oxide (III). If necessary, the N-oxide (II) could be isolated in the pure form; however, this was of no advantage in the further course of the synthesis. In the reduction of 2-ethyl-4-nitropyridine-N-oxide, the nitro group and the N-oxide group were reduced simultaneously to form 2-ethyl-4-aminopyridine (IV) directly. The reduction could be accomplished by different methods; however, the best results were obtained by reduction with iron in a mixture of hydrochloric and acetic acids, when the yield of (IV) reached 90%. We first attempted to prepare 2-ethyl-4-bromopyridine (V) from the amine (IV) by diazotization of (IV) in hydrobromic acid; however, this was unsuccessful. The bromide was obtained by treatment of 2-ethyl-4-aminopyridine perbromide with sodium nitrite in concentrated hydrobromic acid. This method was previously used for the preparation of 2-bromopyridines from 2-aminopyridines [4] and we were the first to use it for the preparation of 4-bromopyridine derivatives. The fear that the side chain of 2-ethyl-4-aminopyridine would be brominated during the preparation of the perbromide was found to be groundless. The reaction proceeded smoothly and the bromide (V) was obtained in very high yield;

we did not detect any side reactions, including bromination of the side chain. For preparation of the nitrile we used a reaction, which was previously used for the preparation of 2- and 3-cyanopyridines [5, 6] and which consists of heating the bromide with cuprous cyanide. The reaction proceeded smoothly at 160-170° and formed a solid complex of the nitrile of 2-ethylisonicotinic acid and cuprous bromide, which was decomposed with ammonia to give the nitrile (VI) in more than 70% yield.

When the bromide (V) was replaced in this reaction by the corresponding chloride by treating 2-ethyl-4-aminopyridine (IV) with sodium nitrite in concentrated hydrochloric acid, 2-ethyl-4-chloropyridine was obtained, but all attempts to condense this with cuprous cyanide to prepare the nitrile (VI) were unsuccessful. In all cases, either the original chloride was recovered or it was completely turned to tar.

The last stage of the synthesis consisted of converting the nitrile (VI) into the thioamide of 2-ethylisonicotinic acid (VII), which was obtained in high yield by saturating a solution of (VI) in pyridine with hydrogen sulfide in the presence of triethylamine. The thioamide obtained was a lemon-yellow crystalline substance, which was slightly soluble in water. To convert it into a water-soluble form, as required for testing, an ether solution of (VII) was saturated with hydrogen chloride to obtain the hydrochloride. The synthesis of the thioamide of 2-ethylisonicotinic acid described is readily reproducible at all stages and is quite convenient from the preparative point of view.

EXPERIMENTAL

2-Ethyl-4-nitropyridine-N-oxide (III). 558 ml of a solution of peracetic acid in acetic acid, containing 54.7 g of peracetic acid (the solution of peracetic acid was stabilized with 5.5 g of concentrated sulfuric acid) was added with stirring to 85 g of 2-ethylpyridine at such a rate that the temperature of the reaction mixture reached 70-80°. The reaction mixture was left overnight and then the solvent removed in vacuum, at first at 40° (25-30 mm) and then on a boiling water bath at 2-3 mm. The sirupy residue of the N-oxide was dissolved in 112 ml of concentrated sulfuric acid and the solution obtained was added to a mixture of concentrated nitric acid (136 ml, d 1.51) and concentrated sulfuric acid (75 ml). The mixture was heated to 100° for 1.5-2 hours, left overnight, poured onto ice and neutralized to a weakly acid reaction with aqueous ammonia. The precipitate was filtered off and the aqueous solution extracted 4-5 times with ether. The ether extracts were dried with sodium sulfate. The ether was evaporated. The residues obtained were combined and recrystallized from water to yield 64.5 g (49%) of 2-ethyl-4-nitropyridine-N-oxide as colorless crystals with m.p. 94-96°. The material was soluble in hot water, hot petroleum ether and readily soluble in alcohols.

Found %: C 49.93, 50.15; H 4.95, 4.89; N 16.86, 16.93. $C_7H_8O_3N_2$. Calculated %: C 49.99; H 4.79; N 16.66.

2-Ethyl-4-aminopyridine. A mixture of 64 g of 2-ethyl-4-nitropyridine-N-oxide, 151 g of iron filings, 190 ml of concentrated hydrochloric acid and 180 ml of acetic acid was boiled with stirring for eight hours and left overnight. The precipitated iron salt was filtered off, the precipitate washed with acetic acid and the filtrate evaporated in vacuum. With cooling, 40% sodium hydroxide solution was added to the residue until the reaction was strongly alkaline, the mixture filtered and the filtrate extracted 6-8 times with ether. The ether extracts were dried with sodium sulfate, the ether removed and the residue vacuum distilled. We obtained 41.4 g (89%) of 2-ethyl-4-aminopyridine as a colorless oil with b.p. 128-130° at 4-5 mm.

Found %: N 22.80, 22.65. $C_7H_{10}N_2$. Calculated %: N 22.93.

Hydrochloride. Dry hydrogen chloride was passed into a solution of 0.5 g of 2-ethyl-4-aminopyridine in 20 ml of absolute ether. The ether was decanted from the precipitated oil and the residue crystallized when fresh ether was added. Recrystallization from absolute butanol yielded colorless crystals with m.p. 54-56°.

Found %: Cl 22.36, 22.22. $C_7H_{11}N_2Cl$. Calculated %: Cl 22.35.

2-Ethyl-4-bromopyridine. 15.4 g of 2-ethyl-4-aminopyridine was dissolved at 10-20° in 40 ml of 50% hydrobromic acid and then 13 ml of bromine was added to the reaction mixture dropwise at −5 to 0° with vigorous stirring. After this, a solution of 21.7 g of sodium nitrite in 31 ml of water was added in the same way and stirring continued for a further half an hour, when a solution of 47 g of sodium hydroxide in 50 ml of water was added at such a rate that the temperature did not rise above 20-25°. The reaction mixture was extracted four times with ether. The extracts were dried with sodium sulfate, the ether removed and the residue vacuum distilled. We obtained 21 g (90%) of 2-ethyl-4-bromopyridine as a colorless oil with b.p. 97-98° at 30 mm.

Found %: C 45.19, 45.30; H 4.57, 4.44; Br 42.81, 42.73. C_7H_8NBr. Calculated %: C 45.17; H 4.33; Br 42.95.

2-Ethyl-4-chloropyridine. 14 g of 2-ethyl-4-aminopyridine was dissolved with cooling in 300 ml of concentrated hydrochloric acid and then saturated with gaseous hydrogen chloride at a temperature of −20 to 30°. After this, 43 g of finely ground sodium nitrite was added to the reaction mixture in small portions and the mixture was left overnight at room temperature. The solution was then evaporated in vacuum, the residue dissolved in water and 40% aqueous sodium hydroxide solution added until a strongly alkaline reaction was produced. The mixture was extracted with ether four times. The extracts were dried with sodium sulfate. The ether was removed and the residue vacuum distilled. We obtained 14 g (86%) of 2-ethyl-4-chloropyridine as a colorless oil with b.p. 76-78° at 18-19 mm.

Found %: C 59.30, 59.35; H 5.82, 5.80; N 10.00, 10.05; Cl 25.12. C_7H_8NCl. Calculated %: C 59.42; H 5.69; N 9.96; Cl 25.06.

Hydrochloride. Dry hydrogen chloride was passed into a solution of 0.5 g of 2-ethyl-4-chloropyridine in 20 ml of absolute ether. The precipitate of hydrochloride was filtered off and recrystallized from anhydrous methanol. The colorless crystals had m.p. 179-180°.

Found %: Cl 39.46. $C_7H_9NCl_2$. Calculated %: Cl 39.89.

Nitrile of 2-ethylisonicotinic acid. A mixture of 21 g of 2-ethyl-4-bromopyridine and 10 g of cuprous cyanide was heated for one hour at 160-170°. The solid reaction mixture obtained was dissolved in 10% ammonia and the mixture extracted with ether four times. The extracts were dried with sodium sulfate, the ether distilled off, and the residue vacuum distilled. We obtained 11 g (73%) of the nitrile of 2-ethylisonicotinic acid as a colorless oil with b.p. 106-110° at 29 mm.

Thioamide of 2-ethylisonicotinic acid. A solution of 11 g of the nitrile of 2-ethylisonicotinic acid in a mixture of 11 g of pyridine and 8.7 g of triethylamine was saturated with hydrogen sulfide for one hour. A yellow, crystalline precipitate formed. The reaction mixture was poured into water and the precipitate collected and washed with water. We obtained 11 g (87%) of the thioamide of 2-ethylisonicotinic acid with m.p. 158-160°. After recrystallization from alcohol, the lemon-yellow needles had m.p. 163-164°. The substance was soluble in alcohol and difficultly soluble in water and ether.

Found %: C 57.91, 58.01; H 6.08, 6.12; N 16.97, 17.12. $C_8H_{10}N_2S$. Calculated %: C 57.79; H 6.06; N 16.85.

Hydrochloride. An ether solution of hydrogen chloride was added to a solution of 5 g of the thioamide of 2-ethylisonicotinic acid in anhydrous alcohol. The crystalline precipitate was filtered off to give the hydrochloride as orange-yellow needles with m.p. 212-214°. The yield was quantitative. The substance was soluble in water and alcohol.

Found %: C 17.56, 17.83. $C_8H_{11}N_2SCl$. Calculated %: C 17.49.

SUMMARY

A convenient preparative method of synthesizing the thioamide of 2-ethylisonicotinic acid, starting from readily available 2-vinylpyridine, is described.

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INVESTIGATION IN THE FIELD OF THIOINDIGOID DYES

II. BROMINATION OF S-ARYLTHIOGLYCOLIC ACIDS

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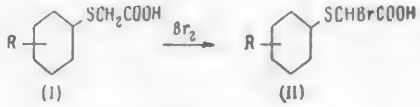
It is known that in the bromination of S-phenylthioglycolic acid [1], its methyl ester [2] and also its derivatives with the para position free [3] in inert solvents, the bromine enters the position para to the sulfur. Under similar conditions, S-(1-bromo-2-naphthyl)-thioglycolic acid was synthesized from S-(β-naphthyl)-thioglycolic acid [4]. When treated with excess bromine in acetic acid, S-(o-nitrophenyl)-thioglycolic acid was converted into dibromomethyl-o-nitrophenylsulfoxide [5]. The formation of α-bromo-S-arylthioglycolic acids by bromination of S-arylthioglycolic acids has been observed by no one if we do not consider the assumption of Pummerer [1] that traces of bromine entered the α-position in the decomposition of the S-dibromide of S-phenylthioglycolic acid. This author obtained α-chloro-S-phenylthioglycolic acid by the action of hydrogen chloride on phenylsulfoxyacetic acid. The use of hydrogen bromide led to the formation of S-(p-bromophenyl)-thioglycolic acid [6].

We studied the bromination of some S-arylthioglycolic acids that we synthesized previously [7]; it was shown that, depending on the reaction conditions, the bromine either entered the nucleus or the methylene group.

By the action of bromine on S-arylthioglycolic acids (I) in carbon tetrachloride or trichlorobenzene, we synthesized a series of α-bromo-S-arylthioglycolic acids (II). It was noticed that radiation accelerated the formation of (II).



(I) (II)

a) R=H b) R=n-CH_3 c) R=n-Br
d) R=o-NO_2 e) R=n-NO_2

In the case of (Ib), however, the methyl group is then involved. The presence of bromine and, especially, a nitro group in the nucleus sharply decreases the reaction rate.

The mechanism put forward for the α-halogenation of thioethers [8], which, in the case of S-arylthioglycolic acids, may be represented by the scheme

$$ArSCH_2COOH \xrightarrow{Br_2} \left[\begin{matrix} Br \\ ArSCH_2COOH \end{matrix}\right]^+ Br^- \xrightarrow{-HBr} Ar\overset{+}{S}Br\overset{-}{C}HCOOH \rightarrow ArSCHBrCOOH,$$

does not explain the acceleration of the reaction by radiation. It has to be assumed that the bromination also proceeds by a radical mechanism.

α-Bromo-S-arylthioglycolic acids are readily cleaved, even by the action of atmospheric moisture, when

*Deceased.

the characteristic smell of thiophenol appears. Under the action of water and aqueous alkali, the bromine is eliminated quantitatively and we used this for analyzing compounds (II) synthesized.

When (II) is boiled with water or, still better, strong hydrochloric acid, bis-(arylthio)-acetic acids (III) are obtained.*

$$ArSCHBrCOOH \xrightarrow{H_2O} ArSH + CHOCOOH \longrightarrow \underset{(III)}{(ArS)_2CHCOOH}$$

The hydrolysis of α-halogenated thioethers proceeds by an analogous scheme [8]. The formation of the thiophenol and the glycolic acid was confirmed by the appearance of the smell of thiophenol and also by the fact that the action of gaseous hydrogen chloride on the thiophenol and the potassium salt of the glycolic acid yielded bis-(phenylthio)-acetic acid [9].

Bromination with the use of catalysts yielded a series of S-arylthioglycolic acids substituted with bromine in the nucleus. It was shown that in the bromination of S-(o-tolyl)- and S-(m-tolyl)-thioglycolic acids, the bromine entered the position para to the sulfur; in the bromination of S-(p-tolyl)-thioglycolic acid, it entered the position ortho to the sulfur and in the bromination of S-(p-methoxyphenyl)- and S-(p-ethoxyphenyl)-thioglycolic acids, it entered the position ortho to the alkoxyl group.

S-(o-Bromophenyl)- and S-(o-carboxyphenyl)-thioglycolic acids were very much more difficult to brominate than S-phenylthioglycolic acid, while we were unable to brominate S-(p-bromophenyl)- and S-(o-nitrophenyl)-thioglycolic acids in the nucleus.

The structures of all the products of nuclear brominations were proved by synthesis.

EXPERIMENTAL

α-Bromo-S-arylthioglycolic acids. 0.02 mole of S-arylthioglycolic acid in 30 ml of carbon tetrachloride was boiled with 0.026 mole of bromine while irradiated with an ultraviolet lamp (75 w) until the bromine in the vapor disappeared (this required one to three hours), and the solution was evaporated to half the original volume and diluted with 50 ml of n-hexane. The α-bromo-S-arylthioglycolic acid was filtered from the cooled mixture. In the case of S-(o-nitrophenyl)- and S-(p-nitrophenyl)-thioglycolic acids, the reaction was performed in 25 ml of trichlorobenzene at 140-160° for half an hour, the mixture cooled, and the α-bromo derivative filtered off and washed with n-hexane.

The product of brominating S-(p-tolyl)-thioglycolic acid with irradiation had a high bromine content (32.9% instead of the calculated 30.60%), probably due to partial bromination of the methyl group; therefore, we prepared α-bromo-S-(p-tolyl)-thioglycolic acid without irradiation.

The results of bromination and the characteristics of the α-bromo-S-arylthioglycolic acids are presented in Table 1.

To elucidate the effect of radiation on the bromination rate, 2.45 g of S-(p-bromophenyl)-thioglycolic acid in 15 ml of carbon tetrachloride was boiled for one hour with 2.1 g of bromine, while the mixture was irradiated with an ultraviolet lamp (75 w) at a distance of 10 cm; the flask used was made of ordinary glass. In addition, an experiment without irradiation was set up. Removal of the solvent in vacuum yielded 1.59 g of α-bromo-S-(p-bromophenyl)-thioglycolic acid, in the first case, and 1.11 g in the second, i.e., in the latter case the bromination rate was lower by a factor of 1.43.

Bromination of S-phenylthioglycolic acid without irradiation yielded a substance with m.p. 105-112°, containing a total of 5% of α-bromo-S-phenylthioglycolic acid. Crystallization from toluene gave S-(p-bromophenyl)-thioglycolic acid with m.p. 117° [1]. With irradiation, α-bromo-S-phenylthioglycolic acid was obtained (Table 1).

Boiling 0.005 mole of the α-bromo-S-arylthioglycolic acids synthesized with 30 ml of hydrochloric acid (d 1.15) for 15 minutes yielded bis-(arylthio)-acetic acids in yields of 90-100% (Table 2). Boiling the original

*In the case of o- and p-nitro substituted α-bromo-S-phenylthioglycolic acids, it was possible to isolate only o- and p-nitrothiophenols.

TABLE 1

Name of acid	Formula	Yield (%)	M.p.	% Br		Notes
				found	calc.	
α-Bromo-S-phenylthioglycolic	$C_8H_7O_2BrS$	45.5	100—102°*	31.8, 31.3	32.32	
α-Bromo-S-(p-tolyl)-thioglycolic	$C_9H_9O_2BrS$	71.5	103.5—104.5**	31.1, 30.3	30.60	Without irradiation
α-Bromo-S-(p-bromophenyl)-thioglycolic	$C_8H_6O_2Br_2S$	87.0	142.5—144***	24.5, 24.1	24.51	The bromine only in a position α to the carboxyl was determined.
α-Bromo-S-(o-nitrophenyl)-thioglycolic	$C_8H_6O_4NBrS$	87.0	138—139***	26.8, 27.1	27.35	
α-Bromo-S-(p-nitrophenyl)-thioglycolic	$C_8H_6O_4NBrS$	91.0	147.5—148.5***	27.05, 26.95	27.35	

*From carbon tetrachloride

**From n-hexane.

***From chlorobenzene.

TABLE 2

Name of acid	Formula	Yield (%)	M.p. (from alcohol)	% S	
				found	calc.
bis-(Phenylthio)-acetic	$C_{14}H_{12}O_2S_2$	100	103—104°*	—	—
bis-(p-Tolylthio)-acetic	$C_{16}H_{16}O_2S_2$	92	127—128	20.45, 20.45	21.07
bis-(p-Bromophenylthio)-acetic	$C_{14}H_{10}O_2Br_2S_2$	87.5	187.5—188	14.38, 14.72	14.77

*Literature data [9]: m.p. 104-106°.

TABLE 3

Substituents in original S-phenylthioglycolic acid	Substituents in S-phenylthioglycolic acid obtained	Formula	Yield (%)	M.p.	% S found	% S calc.	Literature data
H	p-Br	$C_8H_7O_2BrS$	75.3	117°*	—	—	M.p. 118-119° [1]
o-CH_3	5-CH_3, 4-Br	$C_9H_9O_2BrS$	84.4	129—130°*	12.4, 12.3	12.27	
m-CH_3	3-CH_3, 4-Br	$C_9H_9O_2BrS$	82.5	107.5—108°*	12.3, 12.0	12.27	
p-CH_3	2-Br, 4-CH_3	$C_9H_9O_2BrS$	47.0	122—123°*	12.1, 12.2	12.27	M.p. 120°, position of bromine in nucleus not established [1]
p-OCH_3	3-Br, 4-OCH_3	$C_9H_9O_3BrS$	81.3	108—109°**	11.6, 11.5	11.58	M.p. 110-111° [10]
p-OC_2H_5	3-Br, 4-OC_2H_5	$C_{10}H_{11}O_3BrS$	76.7	99.5—100°**	11.2, 11.0	11.03	M.p. 47-48° [10]

*From toluene.

**From water.

with water lowered the yield to 40-60%. Only nitrothiophenols were isolated from the nitro derivatives after this treatment.

S-(Bromoaryl)-thioglycolic acids. Nuclear bromination of S-phenylthioglycolic acid and its methyl and alkoxyl derivatives was accomplished by the following procedure.

In the presence of 0.05 g of iodine, 0.05 mole of bromine was added to 0.05 mole of S-arylthioglycolic acid in 40 ml of chlorobenzene, the temperature raised to 60° and, after the intense evolution of hydrogen bromide had ceased, the mixture cooled to room temperature. In the case of the methyl derivatives, the reaction products which separated were collected by filtration. The S-(alkoxyphenyl)-thioglycolic acid bromo derivatives that were readily soluble in chlorobenzene we collected by treating the reaction mixture with sodium hydroxide solution, distilling off the chlorobenzene and acidifying the alkaline solution.

The results of brominating S-phenylthioglycolic acid and its methyl and alkoxyl derivatives are presented in Table 3.

The structures of the reaction products were proved by synthesis of S-(bromoaryl)-thioglycolic acids by the method described previously [7]. From 2-methyl-4-bromoaniline, 3-methyl-4-bromoaniline, 2-bromo-4-methylaniline, 3-bromo-4-methoxyaniline, and 3-bromo-4-ethoxyaniline we synthesized S-(2-methyl-4-bromophenyl)-thioglycolic acid in 45.7% yield, m.p. 129-130°, S-(3-methyl-4-bromophenyl)-thioglycolic acid in 38% yield, m.p. 107-108°, S-(2-bromo-4-methylphenyl)-thioglycolic acid in 41.6% yield, m.p. 122-123°, S-(3-bromo-4-methoxyphenyl)-thioglycolic acid in 68.3% yield, m.p. 108-109°, and S-(3-bromo-4-ethoxyphenyl)-thioglycolic acid in 71.5% yield, m.p. 99-100°, respectively.

The melting points of mixtures of the acids obtained by bromination and by synthesis were not depressed.

S-(2,4-Dibromophenyl)-thioglycolic acid. To 12.4 g of S-(o-bromophenyl)-thioglycolic acid (obtained from S-(o-aminophenyl)-thioglycolic acid by Sandmeyer's method, yield 57%, m.p. 116-117° (from toluene) [11]) in 100 ml of dichloroethane was added 0.5 g of ferric chloride and 8 g of bromine and the mixture boiled under reflux for two hours. After removal of the dichloroethane, the residue was dissolved in sodium carbonate solution, filtered and acidified to yield 12.9 g of S-(2,4-dibromophenyl)-thioglycolic acid with m.p. 139-140° (from toluene) [7].

S-(2-Carboxy-4-bromophenyl)-thioglycolic acid.

10.6 g of S-(o-carboxyphenyl)-thioglycolic acid, 130 ml of trichlorobenzene, 0.5 g of ferric chloride and 8 g of bromine were heated together to 160°, cooled after ten minutes and filtered. We obtained 9.0 g of S-(2-carboxy-4-bromophenyl)-thioglycolic acid with m.p. 216-217° (from water). By extraction of the mother solution with aqueous sodium hydroxide solution, it was possible to obtain a further 2.6 g of acid.

Found %: Br 27.4, 27.3. $C_9H_7O_4BrS$. Calculated %: Br 27.44.

The substance was the same as S-(2-carboxy-4-bromophenyl)-thioglycolic acid, obtained from 5-bromoanthranilic acid. 2.16 g of 5-bromoanthranilic acid was diazotized, poured at 20° into a solution of 0.74 g of sodium disulfide and 0.6 g of sodium hydroxide in 4 ml of water, heated to boiling, and boiled for one hour. To the cooled solution was added a solution of 2 g of chloroacetic acid, neutralized with sodium carbonate, and the mixture filtered after two hours to yield S-(2-carboxy-4-bromophenyl)-thioglycolic acid; the yield was 56% and the m.p. 216-217° (from water).

Under these conditions, S-(p-bromophenyl)- and S-(o-nitrophenyl)-thioglycolic acids could not be brominated in the nucleus.

SUMMARY

By bromination of S-arylthioglycolic acids with irradiation, previously unknown α-bromo-S-arylthioglycolic acids were synthesized and hydrolysis of these yielded bis-(arylthio)-acetic acids.

A series of S-arylthioglycolic acids, brominated in the nucleus, were synthesized by bromination of S-arylthioglycolic acids in the presence of catalysts.

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SPATIAL STRUCTURE AND REACTIVITY

XIII. THE INTERACTION OF ATOMIC GROUPINGS REMOTE FROM ONE ANOTHER ACCORDING TO THE DATA OF AN INVESTIGATION ON THE KINETICS OF THE REACTION OF BIPHENYL AND STILBENE AMINO DERIVATIVES WITH p-NITROBENZOYL CHLORIDE AND PICRYL CHLORIDE

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Work from our laboratory published previously [1, 2] was devoted to elucidating the nature of the interaction of substituents through a system of two benzene nuclei, joined by a bridge unit. For this purpose, an investigation was made of the kinetics of acylation of amines of the following structure (where M is a bridge atom of oxygen or sulfur):

(I) (II)

A convenient measure for a quantitative evaluation of the conductivity of any molecular system like the systems considered here, with respect to the electronic interaction of two substituents placed at opposite ends, is the ratio of the rate constants for reactions of the mono- and disubstituted derivatives, i.e., K_I/K_{II} (f factor) [1-3]. It was found that atoms of oxygen and sulfur in no way acted as insulators between the benzene nuclei in the molecular systems of diphenyl oxide and diphenyl sulfide. More than that, it was unexpectedly found that, in these systems, the electronic effect of the substituents was transmitted from one benzene ring to the other even better than in the biphenyl system, where these nuclei are connected together directly.

It is well known that replacement of the $-CH=CH-$ group by $-O-$ or $-S-$ atoms in a series of aromatic compounds does not lead to the disappearance of their aromatic properties [4, 5].

In order to develop the hypotheses put forward in our previous work [1, 2], it seemed advantageous to study the reactivity of such amines as (I) and (II) with a vinylene group as M, i.e., appropriate stilbene derivatives.

The problem of how strongly the benzene nuclei interact through a vinylene bridge in the stilbene molecular system has frequently arisen previously in investigations on the color of stilbene and its derivatives [6-10]. According to the data of these investigations, there is considerable conjugation between the benzene nuclei in the stilbene molecular system, as is also confirmed by measuring the intensity of the lines in the Raman spectrum of stilbene [11] and the exaltation of its molecular refraction [12]. On the basis of certain data [8, 11, 12] it can be postulated that the conjugation between the benzene nuclei in stilbene is even more intense than in the biphenyl system. We found nothing in the literature on the investigation of the stilbene molecular system from this point of view by chemical methods, although here one might expect interesting results, the more so as, according to our data [1, 2], chemical and optical methods of investigating similar systems do not always lead to unequivocal results.

In accordance with what is presented above, we studied the kinetics of the reaction of trans-4-aminostilbene, trans-4-amino-4'-nitrostilbene, 4-aminobiphenyl, 4-amino-4'-nitrobiphenyl and aniline with p-nitrobenzoyl

chloride and picryl chloride in benzene solution under exactly the same conditions as were observed in our previous work.* We should note that previously we studied the effect of changing the steric structure of aromatic amines on their reactivity only on the basis of an investigation of the reactions of these amines with the acid chlorides of carboxylic acids and mainly with p-nitrobenzoyl chloride. In the present work, for this purpose we also introduced the reaction of amines with another electrophilic reagent, picryl chloride, which superficially has much in common with the acylation of amines with acid chlorides of carboxylic acids, but at the same time has its own particular characteristics, inherent in the nucleophilic substitution of aromatically bound halogen by an amino group [15, 18]. Without going into details on the fine differences in mechanism of the two reactions, nonetheless, it is necessary to stress the fact that, as is known, in the reactions of amines with acid chlorides, the primary, elementary act of the chemical process is a nucleophilic attack of the carbon atom of the carbonyl by the nitrogen atom of the amino group, while in the case of reactions with picryl chloride, this attack is suffered by a carbon atom of an aromatic nucleus.

The fact that similar results were obtained when the different reactions were used gave us more confidence in arriving at conclusions on the effect of structural and steric factors on the reactivity of the series of compounds investigated.

EXPERIMENTAL

I. Preparation and Purification of Starting Materials

Benzene and p-nitrobenzoyl chloride. The two substances were purified as described previously [19].

Picryl chloride. The technical product, obtained from the Kharkhov chemical-reagent factory, was recrystallized first twice from methyl alcohol (the first time with activated charcoal) and then in the sequence given below: from chloroform (twice), from carbon tetrachloride (2-3 times) and 5-6 times from benzene. The crystals were dried in vacuum at 65°. The melting point of such a sample was 83°, which agrees with literature data [20].

Aniline. The amine hydrochloride (analytical grade) was recrystallized several times from dilute hydrochloric acid (2:1) to a constant melting point equal to 198° [21]. The salt was then decomposed with 50% sodium hydroxide solution, and the amine dried with solid potassium hydroxide and distilled twice at atmospheric pressure (the first time over zinc dust) and, finally, four times in vacuum.

4-Aminobiphenyl. The amine was obtained by the procedure described previously [13] and its hydrochloride purified by further recrystallization from a mixture consisting of one volume of concentrated hydrochloric acid, two volumes of water and three volumes of isopropyl alcohol. After decomposition of the salt with ammonia, the free base was recrystallized several times from aqueous methyl alcohol (1:1) and dried for 12 hours in vacuum at 35-40°. The m.p. was 52°.

4-Amino-4'-nitrobiphenyl. The substance was prepared by a previously described method [13, 19], purified by recrystallization of its hydrochloride from dilute hydrochloric acid (1:1), the salt decomposed with aqueous ammonia, and the amine recrystallized several times from methyl alcohol and 1-2 times from toluene. After drying in vacuum at 100°, the substance had m.p. 205-206°.

Trans-4-aminostilbene. The trans-4-nitrostilbene required for this synthesis was synthesized by the procedure described in [22] and [23] and, as recommended previously [23], in addition to that it was further purified from colored impurities by passing a solution of it in a mixture of benzine and benzene (2:1) through a chromatographic column with aluminum oxide.

3 ml of 98% hydrazine hydrate was added to 3 g of nitrostilbene, obtained by the above method, dissolved in 150 ml of hot ethyl alcohol, and then Raney nickel was added gradually under the conditions which were described in detail previously [24, 25]. After the reaction (the evolution of N_2 ceased after approximately three hours), the solution was filtered in the hot state and the alcohol evaporated to a small residue, to which water was added for more complete separation of the reaction product. The dried amine was dissolved in dry benzene (treated with activated charcoal) and its hydrochloride precipitated by the passage of dry hydrogen chloride into

*Data on the acylation of biphenyl and aniline amine derivatives with p-nitrobenzoyl chloride were taken from our previous work [13, 14].

the solution. The yield of the amine hydrochloride was 2.7 g (87.4%). The salt was recrystallized three times from a mixture consisting of one volume of concentrated hydrochloric acid, two volumes of glacial acetic acid and one volume of water and after this its melting point (with decomposition) equaled 260-262° ([26]: m.p. 245-250°). The salt was decomposed with aqueous ammonia and the free base recrystallized twice from methyl alcohol and once from benzene. After drying in vacuum at 100°, a sample of 4-aminostilbene prepared in this way had m.p. 151-152°, which corresponds to [26]; the acetyl derivative obtained from it was exactly like trans-4-acetylaminostilbene, described in [26].

Trans-4-amino-4'-nitrostilbene. This amino derivative was obtained by partial reduction of 4,4'-dinitrostilbene [23, 27]. In this case it was quite appropriate to use the dinitro compound, which we used in another synthesis [23] and which consisted of a mixture of cis- and trans-isomers with a predominance of the latter, since it is known [28] that the two geometrical isomers of 4,4'-dinitrostilbene give the same product, trans-4-amino-4'-nitrostilbene, on partial reduction.

9 g of trans-4,4'-dinitrostilbene was dissolved in 180 ml of boiling pyridine in a flask, fitted with a reflux condenser. Over a period of five minutes, with the contents of the flask shaken, 54 ml of a molar solution of sodium sulfide in aqueous pyridine* was added. The mixture was boiled carefully for 15 minutes and then 250 ml of cold water added to it. When cool, the precipitated brick-red crystals of the amine were filtered off and washed with water and then with methyl alcohol. The yield was 6.9 g (86.2%). For purification, the amine was recrystallized first from pyridine and then three times from chlorobenzene. Here, it was advantageous to take one and a half times as much solvent as was required to prepare a saturated boiling solution, since the product was very difficultly soluble in cold chlorobenzene. As a result of two further recrystallizations from benzene and drying in vacuum at 100°, the intensively colored crystals of trans-4-amino-4'-nitrostilbene melted at 248-249° (literature data: m.p. 229-230° [29], 245° [28, 30] and 250° [31]).

The method of synthesizing 4-amino-4'-nitrostilbene described above was more advantageous than the similar method of synthesizing it by the partial reduction of 4,4'-dinitrostilbene with sodium hydrosulfide in alcohol solution, since the latter method yielded an impure product due to ethylation of part of the amino derivative formed by alcohol [28].

II. Procedure for Measuring Reaction Rates and Results

There is much in common between the reactions of aromatic amines with acid chlorides of carboxylic acids, on the one hand, and with aromatic halonitro derivatives [15-18], on the other, at least, superficially. Both these reactions are accelerated by the introduction of electron-donating substituents into the aromatic nucleus of the amino derivative and by substitution of the hydrogen atoms of the aromatic nucleus of the acid chloride or halonitro derivative by electron-accepting substituents. Therefore, the halogen atom in picryl chloride, whose molecule contains three nitro groups, is also as labile as that in the acid chlorides of carboxylic acids.

The two reactions proceed by two successive stages (A is any acyl or any aryl residue).

$$A)\ ACl + RNH_2 \rightarrow ANHR + HCl$$

$$B)\ RNH_2 + HCl \rightarrow RNH_2 \cdot HCl$$

or summarizing:

$$C)\ ACl + 2RNH_2 \rightarrow ANHR + RNH_2 \cdot HCl.$$

In both cases, the amine hydrochlorides are unreactive with respect to ACl, whereby the considerably slower first stage (A) determines the second order of the whole over-all process (C).

What has been stated above made it possible to measure the rate of each of the reactions investigated by the same experimental procedure, whose basic characteristics were described in previous communications [14, 32]. In essence, the method mentioned consisted of stopping the reaction a definite moment of time by pouring a

*This was prepared in the following way: 240 g of $Na_2S \cdot 9H_2O$ and 32 g of sulfur was gently heated with 600 ml of water and 100 ml of pyridine until it dissolved completely; the cooled solution was diluted to 1 liter.

benzene solution of diethylamine into the mixture of reacting substances so as to bind the rest of the electrophilic reagent and after this the unreacted aromatic amine was determined by potentiometric titration with sodium nitrite [33]. In the present work we refined the method somewhat (together with D.M. Aleksandrova). Formerly, the amine was titrated after evaporation of the organic solvent, but we found that it was better to proceed in the following way.

After addition of diethylamine to the solution of reacting substances and acidification of the mixture, as indicated [14, 32], with hydrochloric acid, the contents of the reaction flask were carefully washed into the potentiometric-titration flask several times with small portions of glacial acetic acid (a total of ~15-20 ml), and then in exactly the same way with water. To the mixture was added crystalline potassium bromide and a few more drops of hydrochloric acid. The liquid in the flask formed two layers, a benzene and an aqueous one. Therefore it was necessary to ensure that the control electrode and the end of the bridge going to the auxiliary electrode were immersed in the aqueous layer. The titration was performed with vigorous stirring by a mechanical stirrer, which was switched off at the moment of measurement to allow the liquid to form layers as otherwise the results of the determination obtained were less reproducible.

Usually, all the organic substances in the mixture analyzed, with the exception of the aromatic amine hydrochloride, were in the layer of organic solvent or dissolved in the aqueous layer and did not hinder titration. The salt of the amine determined, which was insoluble in benzene (for example, salts of many amines of high molecular weight) may be difficultly soluble in an aqueous medium also. However, experiment showed that this did not interfere with the diazometric determination of these amines under these conditions, as their salts were readily titrated in a suspended state; during the analysis, the titrated liquid gradually cleared and finally became quite transparent.

In order to be satisfied that the reactions we studied proceeded without any side processes and with 100% yield by Eq. (C), before each series of rate measurements we carried out control experiments as recommended in previous communications [14, 32], and, in a number of cases, we also isolated the expected and products, which were identical with samples described in the literature.

TABLE 1

Kinetics of the Reaction of 4-Aminostilbene with p-Nitrobenzoyl Chloride (a = = 0.00125 M, b = 0.0025 M)

25°				50°			
t_i (min)	yield (%)	k_i (l/mol · sec)	n_i	t_i (min)	yield (%)	k_i (l/mol · sec)	n_i
4	14.4	0.283	3	3	24.8	0.761	3
8	24.8	0.277	2	5	35.3	0.752	2
13	35.3	0.281	3	8	46.5	0.750	2
25	50.8	0.277	3	12	56.4	0.746	2
54	69.6	0.284	2	23	71.8	0.766	2
$K_{25°} = 0.280 \pm 0.012$				$K_{50°} = 0.755 \pm 0.012$			

$E = 7600$ cal/mole; $PZ = 1.03 \cdot 10^5$ l/mole · sec; $\Delta S^{\neq} = -37.7$ cal/mol · deg

The rate constants were calculated by the following formula [14, 19, 32] (cf. [16, 17]):

$$K = \frac{1}{2\beta t}\left(\frac{1}{a-x} - \frac{1}{a}\right),$$

where a is the initial concentration of p-nitrobenzoyl chloride or picryl chloride (in moles), x is the decrease in concentration of the given components (in moles) up to moment of time t (in seconds), and β is the correction for the thermal expansion of benzene from 20° to the experimental temperature [19]. This formula was obtained after some transposition of the usual relation for a reaction of the second order, if one considers that, in all our experiments, in accordance with Eq. (C), the initial concentration of amine (b) was always exactly twice the

TABLE 2

Kinetics of the Reaction of 4-Amino-4'-nitrostilbene with p-Nitrobenzoyl Chloride (a = 0.00125 M, b = 0.0025 M)

25°				50°			
t_i (min)	yield (%)	k_i (l/mol · sec)	n_i	t_i (min)	yield (%)	k_i (l/mol · sec)	n_i
24	15.7	0.0520	2	10	14.7	0.119	2
45	26.9	0.0549	2	19	24.8	0.120	2
73	37.1	0.0542	2	30	36.3	0.131	2
163	58.5	0.0581	2	56	51.7	0.132	2
311	74.8	0.0639	3	130	70.8	0.129	2
$K_{25°} = 0.0573 \pm 0.0032$				$K_{50°} = 0.126 \pm 0.005$			

$E = 6000$ cal/mole; $PZ = 1.5 \cdot 10^3$ l/mol · sec ; $\Delta S^{\neq} = -46.0$ cal/mol · deg

TABLE 3

Kinetics of the Reaction of 4-Aminostilbene with Picryl Chloride (a = 0.0025 M, b = = 0.0050 M)

25°				50°			
t_i (min)	yield (%)	k_i (l/mol · sec)	n_i	t_i (min)	yield (%)	k_i (l/mol · sec)	n_i
10	14.8	0.0584	2	5	23.3	0.210	3
20	27.5	0.0635	2	10	38.4	0.215	2
30	35.6	0.0619	2	14	47.8	0.226	2
57	51.9	0.0636	2	20	56.5	0.224	2
90	62.5	0.0620	2	39	73.0	0.239	2
$K_{25°} = 0.0619 \pm 0.0020$				$K_{50°} = 0.222 \pm 0.007$			

$E = 9800$ cal/mole ; $PZ = 9.1 \cdot 10^5$ l/mol · sec; ; $\Delta S^{\neq} = -33.3$ cal/mol · deg

TABLE 4

Kinetics of the Reaction of 4-Amino-4'-nitrostilbene with Picryl Chloride (a = = 0.0025 M, b = 0.0050 M)

25°				50°			
t_i (min)	yield (%)	k_i (l/mol · sec)	n_i	t_i (min)	yield (%)	k_i (l/mol · sec)	n_i
30	10.6	0.0132	3	14	15.3	0.0445	3
60	17.9	0.0122	2	27	24.9	0.0424	3
145	33.4	0.0116	2	44	35.6	0.0433	2
270	48.1	0.0115	2	82	49.7	0.0416	2
630	68.7	0.0117	3	190	69.7	0.0418	3
$K_{25°} = 0.0121 \pm 0.0005$				$K_{50°} = 0.0428 \pm 0.0009$			

$E = 9700$ cal/mole, $PZ = 1.5 \cdot 10^5$ l/mole · sec ; $\Delta S^{\neq} = -36.9$ cal/mol · deg

TABLE 5

Kinetics of the Reaction of 4-Aminobiphenyl with Picryl Chloride (a = 0.0025 M, b = 0.0050 M)

25°				50°			
t_i (min)	yield (%)	k_i (l/mol · sec)	n_i	t_i (min)	yield (%)	k_i (l/mol · sec)	n_i
7	13.8	0.0767	2	5	25.1	0.231	2
14	24.3	0.0768	3	8	34.9	0.231	2
23	34.0	0.0751	2	12	45.5	0.240	2
42	47.1	0.0711	2	18	55.4	0.238	3
99	67.7	0.0710	2	35	70.3	0.234	2
$K_{25°} = 0.0744 \pm 0.0021$				$K_{50°} = 0.235 \pm 0.003$			

$E = 8800$ cal/mole; $PZ = 2.1 \cdot 10^5$ l/mol · sec ; $\Delta S^{\neq} = -36.2$ cal/mol · deg

TABLE 6

Kinetics of the Reaction of 4-Amino-4'-nitrobiphenyl with Picryl Chloride (a = 0.0025 M, b = 0.0050 M)

25°				50°			
t_i (min)	yield (%)	k_i (l/mol · sec)	n_i	t_i (min)	yield (%)	k_i (l/mol · sec)	n_i
100	15.2	0.00598	2	15	8.9	0.0225	2
177	23.4	0.00580	2	51	23.4	0.0207	2
322	34.1	0.00540	3	82	32.3	0.0201	2
600	48.5	0.00527	3	152	47.3	0.0204	2
900	58.4	0.00522	3	464	71.5	0.0187	2
$K_{25°} = 0.00548 \pm 0.00018$				$K_{50°} = 0.0205 \pm 0.0009$			

$E = 10000$ cal/mole; $PZ = 1.38 \cdot 10^5$ l/mol · sec; $\Delta S^{\neq} = -37.1$ cal/mol · deg

TABLE 7

The Kinetics of the Reaction of Aniline with Picryl Chloride (a = 0.0025 M, b = 0.0050 M)

25°				50°			
t_i (min)	yield (%)	k_i (l/mol · sec)	n_i	t_i (min)	yield (%)	k_i (l/mol · sec)	n_i
5	15.0	0.118	2	3	25.4	0.392	2
10	26.4	0.120	3	5	35.9	0.387	3
15	35.7	0.124	2	8	47.9	0.397	2
25	46.6	0.117	2	13	60.2	0.401	2
38	57.6	0.120	2	20	69.6	0.396	2
60	68.2	0.120	2				
$K_{25°} = 0.120 \pm 0.002$				$K_{50°} = 0.394 \pm 0.005$			

$E = 9100$ cal/mole; $PZ = 5.6 \cdot 10^5$ l/mol · sec; $\Delta S^{\neq} = -34.3$ cal/mol · deg

TABLE 8

Collected Data on the Kinetics of the Reactions of Amines with p-Nitrobenzoyl Chloride and Picryl Chloride*

Amine	Electrophilic agent**	$K_{25°}$	$K_{50°}$	E	PZ	$\Delta S^{\neq}$
	PNBC	0.280 ± 0.012	0.755 ± 0.012	7600	1.03 · 10⁵	—37.7
	PC	0.0619 ± 0.0020	0.222 ± 0.007	9800	9.1 · 10⁵	—33.3
	PNBC	0.0573 ± 0.0032	0.126 ± 0.005	6000	1.5 · 10³	—46.0
	PC	0.0121 ± 0.0005	0.0428 ± 0.0009	9700	1.5 · 10⁵	—36.9
	PNBC	0.533 ± 0.010	1.11 ± 0.02	5600	7.1 · 10³	—42.8
	PC	0.0744 ± 0.0021	0.235 ± 0.003	8800	2.1 · 10⁵	—36.2
	PNBC	0.0505 ± 0.0011	0.118 ± 0.003	6500	2.9 · 10³	—44.7
	PC	0.00548 ± 0.00018	0.0205 ± 0.0009	10000	1.38 · 10⁵	—37.1
	PNBC	0.580 ± 0.018	—	—	—	—
	PC	0.120 ± 0.002	0.394 ± 0.005	9100	5.6 · 10⁵	—34.3

*The dimensions of the values are the same as in Tables 1-7.

**PNBC – p-nitrobenzoyl chloride, PC – picryl chloride.

concentration of the electrophilic reagent (a) reacting with it. The accuracy of the values calculated for the rate constants was evaluated by mathematical statistics [34] (0.95 reliability).

The activation energy (E), the frequency factor (PZ) and the activation entropy (ΔS^{a}) were calculated exactly as described previously [14, 32].

The numerical data obtained for the reactions investigated in this work are given in Tables 1-7, where the following symbols are used: k_i and K are the respective average values for the rate constants, first for the given interval of time t_i over n_i measurements and second, for all Σn_i measurements. The average values of the reaction yields for n_i measurements are given in the second column of these tables.

Table 8 summarizes the main data on the kinetics of the reactions investigated in this work as well as certain values for reactions we had studied previously.

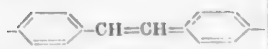
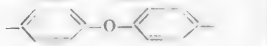
DISCUSSION OF RESULTS

The wide investigations of V.A. Izmail'skii et al. [9, 10] on the color of a wide range of compounds of types (I) and (II) (and others similar to them) in the solid state and in various solvents showed that the intramolecular interaction of atoms and atomic groups in these compounds appears most clearly in an inert solvent medium. If such substances are in a crystalline state or dissolved in polar solvents, then this effect is masked by factors caused by molecular association (exomolecular interaction [9, 10]), whose role may predominate in certain cases. Taking this into consideration, one may assume that, in our experiments in dilute benzene solutions, the intermolecular interactions between similar molecules of the reaction substances may be neglected; consequently, all the effects observed, which are connected with changes in reactivity of the amino derivatives studied in this work, should be considered as due to only intramolecular (endomolecular [9, 10]) factors.

The results given in Table 8 show that the electronic effect of the phenyl group, introduced into the para position of the aniline molecule, shows quantitative differences in reactions with the two electrophilic reagents. While, in going from aniline to 4-aminobiphenyl, the rate constant hardly changes noticeably in reactions with p-nitrobenzoyl chloride, in reactions of these amines with picryl chloride, the rate changes in

TABLE 9

Values of the f Factors for the Molecular Systems of Stilbene, Biphenyl, Diphenyl Oxide and Diphenyl Sulfide

System	f_{25}* for reaction with p-nitrobenzoyl chloride	f_{25}* for reaction with picryl chloride
	4.9	5.1
	10.6	13.6
	12.1[1]	—
	23.8[2]	—

the same direction, but quite considerably. This result agrees with the fact that the reactions of aromatic amines with halonitro derivatives of the benzene series are more sensitive to structural changes in the molecules of the amine derivatives than the analogous reactions with acid chlorides of carboxylic acids: reactions with halonitro derivatives are characterized by particularly high values of the Hammett constant ρ* [35].

A comparison of the results of the reactions of aniline and 4-aminostilbene with the two electrophilic reagents shows that the group p-$C_6H_5-CH=CH-$ has a more sharply expressed electron-accepting nature than the group p-C_6H_5-. However, it is interesting that, according to the data of Kochi and Hammond [36], obtained by a study of various reactions (solvolysis of benzyl tosylates, measurement of the dissociation constants of carboxylic acids and alkaline hydrolysis constants of their esters), this grouping, on the contrary, behaves as an electron donor. Apparently, the action of this group on the aromatic ring (like the p-phenyl also) may change, depending on the character of the reaction. The electron-accepting effect of such para substituents as p-$NO_2C_6H_4-$ and p-$NO_2C_6H_4-CH=CH-$ is even more clearly expressed. Their introduction into the aniline molecule leads to an extremely substantial fall in the reactivity of the aromatic amino group.

The value of the f factor for the molecular system of stilbene both in the case of the reaction with p-nitrobenzoyl chloride and with picryl chloride was found to be a factor of approximately two less than the value of f for the analogous system of biphenyl (Table 9). This indicates that the molecular system of biphenyl is a better conductor of the electronic interaction of the substituents than the stilbene system.

Despite the fact that the bridge grouping, $-CH=CH-$, connecting the two benzene nuclei, contains mobile π-electrons, it is a considerably worse conductor of electronic effects than analogous bridges of the atoms $-O-$ and, especially, $-S-$. Thus, for example, the value of the f factor for the molecular system of stilbene (reaction with p-nitrobenzoyl chloride) is a factor of two and a half less than that for the diphenyl oxide system, and a factor of almost five less than that for the diphenyl sulfide system. Thus, atoms of $-O-$ or $-S-$, introduced into a conjugated chain in place of the grouping $-CH=CH-$, in no way behave as insulators of electronic interaction. This conclusion appears to be in contradiction to the results of optical investigations of similar systems (see literature on this problem cited in [1] and [9], pp 91-92). However, as we noted previously [1], this contradiction is only apparent since, by themselves, optical methods do not allow a sufficiently complete characterization of the interactions of substituents in the molecular systems interesting us.

As regards the question of whether the bridging vinylene grouping is a worse conductor of electronic effects than analogous atoms of oxygen and sulfur, it seems to us that it is difficult to answer this question completely at the present time. However, it is apparently necessary to take note of the following considerations. Transmission of the electronic interaction of substituents in the molecular system of stilbene from one benzene nucleus to the other through the vinylene grouping must be achieved by two mechanisms, inductive and due to the effect of π,π-conjugation (cf. [1, 2, 38]). In the case of the molecular systems of diphenyl oxide and diphenyl sulfide, instead of the latter effect, there is p,π-conjugation. Thus, in going from the stilbene system to the two other systems considered, at least two factors change essentially: first, the nature of the conjugation effect is changed and, second, the unit connecting the benzene nuclei is shortened by a factor of approximately two. While it is difficult to evaluate the role of the first factor at the moment, we may nonetheless state, with sufficient confidence, that the latter factor, which facilitates the appearance of an induction mechanism, must undoubtedly be of great importance in the given case.

The increased role of an induction mechanism also explains why the molecular system of biphenyl is a better transmitter of electronic interaction of substituents than the stilbene system, which is longer than it by two methyne units.

*As is known, this constant serves as a measure of the ease with which a particular aromatic system transmits the electronic interaction of the substituents, appearing in any concrete reaction.

The comparative investigation we carried out on the properties of compounds with the bridge units $-CH=CH-$ $-O-$, $-S-$, connecting benzene nuclei, also shows that there is a quite definitely expressed analogy between these properties and the role which the heteroatoms play in heterocyclic compounds with an aromatic character (furan and thiophene).

As regards the energy indexes of the reactions investigated in the present work, one may state that the reactions proceed at very low values of activation energy and entropy and it should be noted that the reactions with picryl chloride are characterized by somewhat higher values of these kinetic parameters than the analogous reactions with p-nitrobenzoyl chloride. The following should be noted: in going from 4-aminobiphenyl to its 4'-nitro derivative, besides a decrease in rate, there is an increase in activation energy, while, in the case of reactions of similar stilbene derivatives, the opposite is observed.

SUMMARY

1. A study was made of the kinetics of the reactions of aniline, 4-aminobiphenyl, 4-amino-4'-nitrobiphenyl, 4-aminostilbene and 4-amino-4'-nitrostilbene with p-nitrobenzoyl chloride and picryl chloride in a benzene solution.

2. It was shown that the molecular system of stilbene, in which the benzene nuclei are separated by a vinylene bridge grouping, is a worse conductor of electronic effects (from one nucleus to the other) than the biphenyl system, in which the benzene nuclei are bound directly to each other.

3. The vinylene bridge grouping between the benzene nuclei in the molecular system of stilbene transmits electronic effects from one nucleus to another considerably worse than the analogous oxygen and, especially, sulfur atoms in the diphenyl oxide and diphenyl sulfide systems.

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UNSYMMETRICAL PYRIDINE DYES

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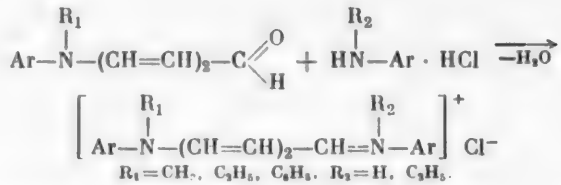
It was noted long ago that the color of unsymmetrical dyes could be imagined as a "molecular mixture" of the colors of the corresponding symmetrical dyes; however, the color of an unsymmetrical dye is not always additive. The relation between the color and the asymmetry of the molecule was studied systematically for cyanine dyes [1]. A.I. Kiprianov and G.T. Pilyugin [2] first established that additivity in color was only shown by those dyes in which the terminal units of the chromophore were heterocyclic bases, similar in basicity. A difference in the basicity of the amines forming the dye produces a shift in the absorption maximum from the calculated additive value, more frequently toward the short-wave part of the spectrum. Later, a similar rule was observed by Brooker [3] in the color of unsymmetrical dyes of various classes. In subsequent work, A.I. Kiprianov et al. [4] and G.T. Pilyugin et al. [5] showed that the relation found was obeyed by a large number of examples. The authors explained the hypsochromic shift in the absorption maximum by a disturbance of the equalization of the bonds in the conjugated system due to the difference in the basicity of the terminal units, the heterocyclic amines.

We investigated the absorption spectra of 17 unsymmetrical pyridine dyes, obtained by Zincke's method [6], by the condensation of N-substituted monoanils of glutaconic aldehyde with aromatic amines in the presence of acid by the known scheme



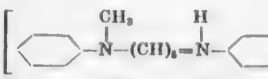
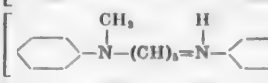
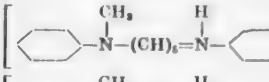
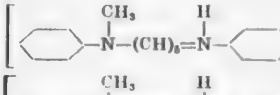
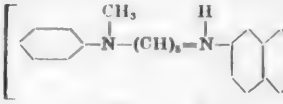
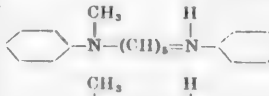
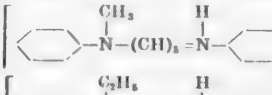
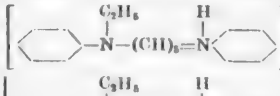
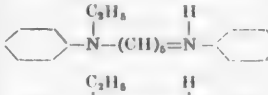
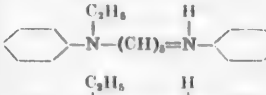
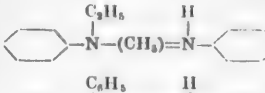
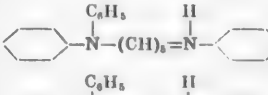
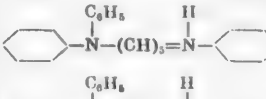
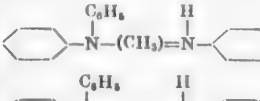
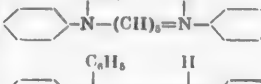
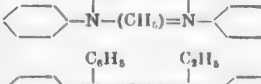
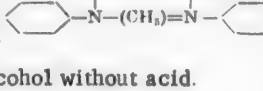
$R_1 = CH_3$, C_2H_5, C_6H_5. $R_2 = H$, C_2H_5.

It was established previously [7] that pyridine dyes, which are derivatives of primary aromatic amines, undergo hydrolysis and the color of the alcohol solutions is sometimes increased; hydrochloric acid was added to the alcohol solutions to suppress hydrolysis. The absorption spectra of unsymmetrical dyes, containing primary amine residues, were determined in ethyl alcohol in the presence of hydrochloric acid (with the exception of diamine derivatives).

Table 1 shows the data from optical determinations for unsymmetrical and the corresponding symmetrical pyridine dyes in 95% ethyl alcohol in the presence of hydrochloric acid. The values of the maxima of the symmetrical dyes, derivatives of secondary amines, are presented in the column with the number I, those of the primary amine derivatives in the column with the number II and the calculated additive maximum in the column with the heading [(I) + (II)]/2.

Comparison of the data in the table shows that eight dyes (2, 3, 5, 8, 10, 12, 13, 16) conform to additivity in color (allowing a deviation of ±5 mμ), for six of the dyes (1, 4, 6, 7, 11, 14) a hypsochromic shift from the additive maximum is observed and for three of the dyes (9, 15, 17) the maximum is shifted toward longer wavelengths. The reason for the bathochromic shift of the absorption maximum of unsymmetrical dyes is unclear.

TABLE 1

Sample No.	Formulas of unsymmetrical dyes	λ_{max} (mμ)/ε · 10⁻⁴ unsymmetrical	sym-metrical (I)	sym-metrical (II)	$\frac{(I)+(II)}{2}$	Deviation from additive max. (mμ)
1		465/4.6	450/8.0	487/12.6	476/10.3	−11
2		475/7.0	450/8.0	495/9.8	473/8.9	+2
3		470/7.8	450/8.0	500/8.0	475/8.0	−5
4		515/5.6	450/8.0	567/8.0	541/8.0	−26
5		478/6.1	450/8.0	510/10.8	480/9.4	−2
6		470/4.6	450/8.0	500/6.3	485/7.1	−15
7		480*/—	450/8.0	527/—	489/—	−9
8		466/6.3	442/6.7	487/12.6	465/9.6	+1
9		476	442/6.7	495/9.8	468/8.3	+8
10		474	442/6.7	500/8	471/7.4	+3
11		475/7.4	442/6.7	527/—	484.5	−9.5
12		485/4.8	487/6.4	487/12.6	487/9.5	−2
13		489/4.5	487/6.4	495/9.8	491/8.1	−2
14		480/3.1	487/6.4	500/8.0	493/7.2	−13.5
15		535*/4.4	487/6.4	567*/8.0	527/7.2	+8
16		503/—**	487/6.4	527/**—	507/—	−4
17		489/5.2	487/6.4	442/6.7	$\frac{464.5}{6.5}$	+24.5

*In alcohol without acid.

**In glacial acetic acid.

TABLE 2

Sample No.	Name of dye (chloride)	Yield of dye (%)	External form of crystals	M.p.	Analysis data		
					formula	found (%)	calc. (%)
1	1-(N-Methylphenylamino)-5-(phenylamino)-pentadiene-1,3 [6]	60	Fine red needles with a bluish luster (from methanol)	166°	$C_{18}H_{19}N_2Cl$	Cl 10.52, N 9.39, 9.34	Cl 10.73, N 9.38
2	1-(N-Methylphenylamino)-5-(p-methylphenylenamino)-pentadiene-1,3	45	Red-violet needles (from ethanol)	130	$C_{19}H_{21}N_2Cl$	Cl 8.56, N 8.93, 8.94	Cl 8.77, N 8.96
3	1-(N-Methylphenylamino)-5-(p-methoxyphenylenamino)-pentadiene-1,3	56	Brown-red (from ethanol)	128	$C_{19}H_{21}ON_2Cl$	N 8.47, 8.54	N 8.52
4	1-(N-Methylphenylamino)-5-(p-diethylaminophenylenamino)-pentadiene-1,3	40	Dark violet with green luster (from acetone)	125	$C_{22}H_{23}N_2Cl$	N 11.25, 11.4	N 11.37
5	1-(N-Methylphenylamino)-5-(β-naphthylamino)-pentadiene-1,3	50	Fine red (from mixture of ethanol and ether)	126	$C_{22}H_{21}N_2Cl$	N 7.93, 8.0	N 8.03
6	1-(N-Methylphenylamino)-5-(p-carbethoxyphenylenamino)-pentadiene-1,3	40	Fine red-violet (from ethanol)	162	$C_{19}H_{19}O_2N_2Cl$	N 8.00, 8.32	N 8.20
7	1-(N-Methylphenylamino)-5-(p-nitrophenylenamino)-pentadiene-1,3	46	Fine brown (from 60% methanol)	114	$C_{18}H_{18}O_2N_3Cl$	N 12.3, 12.35	N 12.23
8	1-(N-Ethylphenylamino)-5-(phenylamino)-pentadiene-1,3	70	Red (from acidified aqueous ethanol)	121	$C_{19}H_{21}N_2Cl$	N 8.92, 8.96	N 8.90
9	1-(N-Ethylphenylamino)-5-(p-methylphenylenamino)-pentadiene-1,3	55	Fine red (from acidified aqueous ethanol)	110	$C_{20}H_{23}N_2Cl$	N 9.5, 9.58	N 9.3

TABLE 2 (continued)

Sample No.	Name of dye (chloride)	Yield of dye (%)	External form of crystals	M.p.	Analysis data		
					formula	found (%)	calc. (%)
10	1-(N-Ethylphenylamino)-5-(p-methoxyphenylenamino)-pentadiene-1,3	71	Red-violet (from methanol with hydrochloric acid)	115°	$C_{20}H_{23}ON_2Cl$	N 7.26, 7.42	N 7.18
11	1-(N-Ethylphenylamino)-5-(p-nitrophenylenamino)-pentadiene-1,3	34	Brown with green luster	139	$C_{19}H_{20}O_2N_3Cl$	N 10.55, 10.6	N 10.3
12	1-(N-Diphenylamino)-5-(phenylamino)-pentadiene-1,3	80	Orange red (from acidified aqueous ethanol)	136	$C_{23}H_{21}N_2Cl$	N 7.6, 7.65	N 7.7
13	1-(N-Diphenylamino)-5-(p-methylphenylamino)-pentadiene-1,3	60	Orange red (from acidified aqueous ethanol)	137	$C_{24}H_{23}N_2Cl$	N 7.6, 7.7	N 7.48
14	1-(N-Diphenylamino)-5-(p-methoxyphenylenamino)-pentadiene-1,3	35	Fine red (from acidified aqueous ethanol)	120	$C_{24}H_{23}ON_2Cl$	N 6.97, 7.1	N 7.18
15	1-(N-Diphenylamino)-5-(p-diethylaminophenylenamino)-pentadiene-1,3	41	Lustrous red-violet (from acidified methanol)	146	$C_{27}H_{30}N_3Cl$	N 10.0, 9.94	N 9.73
16	1-(N-Diphenylamino)-5-(p-nitrophenylenamino)-pentadiene-1,3	55	Fine red (from acetic acid with hydrogen chloride)	150	$C_{23}H_{20}O_2N_3Cl$	N 10.41, 10.61	N 10.37
17	1-(N-Diphenylamino)-5-(N-ethylphenylamino)-pentadiene-1,3	50	Red (from acidified ethanol)	142	$C_{25}H_{25}N_2Cl$	N 7.37, 7.23	N 7.20

It is curious that the tendency for a bathochromic shift in the absorption maximum is observed in all cases where the basicity of the primary amine is increased (cf. 8 and 9 and 14 and 15); however, the strongest bathochromic shift in the absorption maximum is observed for dye 17, which is formed of two secondary amines, differing strongly in basicity and having steric hindrance. In the case of a bathochromic shift in the maximum of an unsymmetrical dye, there is sometimes a considerable decrease in the absorption intensity. The color of dye 17 hardly differs from the color of the more deeply colored symmetrical dye which, like the more highly colored one, has steric hindrance, though it would hardly disturb the planarity of the molecule's structure; it is possible that the bonds are deformed in these molecules, i.e., the bond angles of the atoms are deformed [8] and, due to this, the energy level of the excited state of the molecule is lowered and the color deepened. Deformation of the angles must hinder equalization of the bonds, i.e., displacement of the π-electrons in the conjugated system and, therefore, the absorption intensity is decreased. However, the hypothesis presented for the reason for the different shift in the absorption maximum of unsymmetrical dyes from the calculated additive value does not explain why, in one case, the steric hindrance disturbs the planar structure of the molecule and, in the other, it produces a deformation of the bonds between the atoms without disturbing the planar structure of the molecule. Further investigations in this direction are required.

EXPERIMENTAL

The unsymmetrical pyridine dyes were obtained by the general method [6]. An equimolecular mixture of the monoanil of glutaconic aldehyde and amine was moistened with several drops of alcohol or acetic acid, heated on a water bath at 60-80° for 1-2 minutes and diluted with hydrochloric acid (1 ml of HCl, d 1.19, to 5 ml of H_2O). The precipitate was collected and washed on the filter with very dilute acid, pressed out well and washed with ether. Concentrated acid may be added to the mixture of monoanil and amine, but it must be borne in mind that excess acid decomposes the monoanil and symmetrical dyes may be formed. The best yields of dyes were obtained in condensation of amine hydrochlorides with the monoanils in a small amount of alcohol or acetic acid. In general, the unsymmetrical dyes were very soluble in alcohol and acetic acid. They were purified by recrystallization from alcohol acidified with hydrochloric acid, or from alcohol diluted with water and acidified. Prolonged heating of the acidified solutions is not recommended since the dyes are not stable. The unsymmetrical dyes could be freed from possible traces of symmetrical dyes by repeated recrystallization. With similar melting points for the unsymmetrical and the corresponding symmetrical dyes, the melting point of a mixture of them was determined. Before analysis, the dyes were dried in vacuum over phosphorus pentoxide at 50-65°. Data on the dyes synthesized are given in Table 2. The monoanils of glutaconic aldehyde, required for the synthesis of the unsymmetrical dyes, were described in another place [9].

SUMMARY

1. Seventeen unsymmetrical pyridine dyes were synthesized and, of these, sixteen are not described in the literature.

2. In most cases, the relation between the change in color and the change in basicity of the amines, forming the molecule of the unsymmetrical dye, established by A.I. Kiprianov and G.T. Pilyugin, was observed on comparing the absorption spectra of the unsymmetrical and the corresponding symmetrical dyes.

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•Original Russian pagination. See C.B. translation.

SYNTHESES OF SELENOORGANIC COMPOUNDS, PROCEEDING FROM CARBON DISELENIDE

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The purpose of the present work was the synthesis of certain new selenium compounds from carbon diselenide.

Carbon diselenide is one of the most accessible and simplest selenium compounds of carbon. It is formed on reaction of carbon tetrachloride with phosphorus pentaselenide [1, 2], cadmium selenide [3], or hydrogen selenide [4], and also on heating elementary selenium with methylene chloride in a current of nitrogen [5]. The last method of preparing carbon diselenide is the best.

Carbon diselenide readily reacts with chlorine to form trichloromethylselenium chloride [5].

$$CSe_2 \xrightarrow{Cl_2} CCl_3SeCl$$

When this reaction is carried out at low temperatures, the yield of trichloromethylselenium chloride may be increased to 73%. We found that trichloromethylselenium chloride readily reacts with potassium cyanide to form trichloromethylselenocyanate.

$$CCl_3SeCl \xrightarrow{KCN} CCl_3SeCN$$

Trichloromethylselenium chloride reacts with ethylene to give trichloromethyl-β-chloroethyl selenide.

$$CCl_3SeCl \xrightarrow{CH_2=CH_2} CCl_3SeCH_2CH_2Cl$$

On reduction of trichloromethylselenium chloride with metallic tin in a hydrochloric acid medium, a dimer of selenocarbonyl chloride is obtained.

$$CCl_3SeCl \xrightarrow{Sn} (CCl_2Se)_2$$

Carbon diselenide reacts with selenium dioxide to form carbon oxyselenide

$$CS_2 \xrightarrow{SeO_2+\text{oleum}} CSeO$$

EXPERIMENTAL

Trichloromethylselenium chloride. Into a flask provided with a low-temperature thermometer was put a solution of 17 g of carbon diselenide in 100 ml of carbon tetrachloride, and 28.5 g of dry chlorine was slowly added with cooling to −80 to −30° and constant stirring. In the course of the reaction the solution became red, and selenium tetrachloride settled to the bottom of the flask. After addition of the calculated quantity of chlorine, the reaction mixture was slowly heated to room temperature and left for several hours. Then the precipitate was filtered out, and the carbon tetrachloride was distilled from the liquid at a reduced pressure about 200 mm. The liquid remaining in the flask was quickly washed with an equal volume of water, dried with calcium chloride, and distilled. There was obtained 17 g (73%) of trichloromethylselenium chloride.

B.p. 68° at 23 mm, $n^{21}D$ 1.5808, d^{21}_{21} 2.1140.

Found %: C 5.56, 5.43; Cl 60.61, 60.82; Se 33.59, 33.75. CCl_4Se. Calculated %: C 5.16; Cl 60.94; Se 33.90.

Trichloromethyl selenocyanate. To a solution of 3.5 g of trichloromethylselenium chloride in 5.0 ml of carbon tetrachloride was added 1 g of a solution of potassium cyanide in 1 ml of water in small portions with stirring and cooling (temperature not over +5°). In the course of the reaction the color of the solution changed from bright-red to light-yellow, and potassium chloride was precipitated. After completion of the reaction, the liquid was filtered, dried with sodium sulfate and distilled. There was obtained 2.1 g (63%) of trichloromethyl selenocyanate.

B.p. 88° at 20 mm, $n^{25}D$ 1.5564, d^{25}_4 1.993.

Found %: C 11.01, 11.36; Cl 47.42; Se 35.35, 35.26. C_2Cl_3NSe. Calculated %: C 10.71; Cl 47.65; Se 35.35.

Trichloromethyl-β-chloroethyl selenide. Into a test tube provided with inlet and outlet tubes was put 3.5 g of trichloromethylselenium chloride. The inlet tube was connected to a gas reservoir filled with ethylene; the latter was blown through the apparatus until air was completely removed, and the outlet tube was closed. The absorption of the calculated quantity of ethylene lasted for several hours, the entire reaction taking place with the outlet-tube stopcock closed.

The trichloromethylselenium chloride, initially deep-red, gradually lightened as the reaction proceeded, and became light-yellow. On distillation trichloromethyl-β-chloroethyl selenide was obtained in quantitative yield.

B.p. 108° at 7 mm, $n^{20}D$ 1.5722, d^{20}_4 1.874.

Found %: C 13.89, 13.90; H 1.90, 1.56; Cl 54.09, 54.48; Se 30.24, 30.18. $C_3H_4Cl_4Se$. Calculated %: C 13.80; H 1.54; Cl 54.40; Se 30.26.

Carbon oxyselenide. 20 g of carefully dried selenium dioxide and 5 g of carbon diselenide were heated in an open flame for 3-5 minutes until a homogeneous mixture was obtained. Then, after cooling to room temperature, 10 ml of oleum was added dropwise to the reaction mixture. The reaction proceeded very vigorously with precipitation of elementary selenium. The evolved gases were collected in a receiver cooled with liquid air. After the reaction was finished, the gases were distilled through a column for low-boiling substances. There was obtained 0.51 g (16%) of carbon oxyselenide, b.p. −22, −20°.

Found %: Se 73.00. COSe. Calculated %: Se 73.83.

SUMMARY

1. A method of preparation of trichloromethylselenium chloride through the chlorination of carbon diselenide at low temperatures has been studied.

2. New selenoorganic compounds have been synthesized: trichloromethyl selenocyanate and trichloromethyl-β-chloroethyl selenide.

3. It has been established that carbon diselenide reacts with selenium dioxide to form carbon oxyselenide.

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PREPARATION OF HEXAFLUORODIMETHYL DISELENIDE FROM SALTS OF TRIFLUOROACETIC ACID, AND SOME OF ITS PROPERTIES

N.N. Yarovenko, V.N. Shemanina and G.B. Gazieva

Lately, as is generally known, decarboxylation reactions of salts of fluorinated organic acids have been widely used for the synthesis of organofluorine compounds [1, 2]. The reactions apparently take place according to the schemes

$$CF_3CO_2Ag \xrightarrow{Hal_2} [CF_3CO_2Hal] \rightarrow CF_3Hal$$

$$CF_3CO_2Ag \xrightarrow{ClNO} [CF_3CO_2NO] \rightarrow CF_3NO$$

However, on decarboxylation of trifluoroacetic acid salts in the presence of sulfur there are formed not organofluorine compounds of sulfur, but sulfur dioxide, silver sulfide, and trifluoroacetic anhydride [3].

$$4CF_3CO_2Ag + 3S = 2Ag_2S + 2(CF_3CO)_2O + SO_2$$

In view of the fact that selenium is an analog of sulfur and has many properties in common with it, it seemed unlikely that organofluorine compounds of selenium could be prepared in such a way. For this reason, decarboxylation of salts of fluorinated acids in the presence of selenium has not been carried out by anyone until now.

We found that when mercuric or silver trifluoroacetate is heated with selenium, the reaction proceeds otherwise than with sulfur, and hexafluorodimethyl diselenide is formed.

$$(CF_3CO_2)_2Hg \xrightarrow{Se} CF_3SeSeCF_3$$

The reaction products must be collected by means of liquid air, since, if the receiver is insufficiently cooled, a considerable part of the diselenide is carried away by the carbon dioxide evolved during the reaction.

As is generally known, the preparation of hexafluorodimethyl diselenide and hexafluorodimethyl selenide by heating trifluoroiodomethane with selenium is mentioned in the cited reviews on organofluorine compounds [1, 2].

$$CF_3I \xrightarrow{Se} (CF_3)_2Se_2 + (CF_3)_2Se$$

Five products of their further conversion also are described: CF_3SeCl, CF_3SeCl_3, CF_3SO_2H, $CF_3SeHgCl$, $CF_3SeHgSeCF_3$. The hexafluorodimethyl diselenide obtained by us was cleaved by chlorine and bromine according to the scheme

$$CF_3SeSeCF_3 \xrightarrow{Hal_2} CF_3SeHal$$

As was to be expected, the trifluoroalkylselenium halides obtained proved to be very reactive compounds. They readily react with potassium cyanide to form selenocyanates.

$$CF_3SeCl \xrightarrow{KCN} CF_3SeCN$$

They readily add to unsaturated compounds to form trifluoromethyl-β-chloroalkyl selenides.

$$CF_3SeCl \xrightarrow{CH_2=CH_2} CF_3SeCH_2CH_2Cl$$

They react with acetone to form trifluoromethyl acetonyl selenide.

$$CF_3SeCl \xrightarrow{CH_3COCH_3} CF_3SeCH_2COCH_3$$

EXPERIMENTAL

Hexafluorodimethyl diselenide. 10 g of colloidal selenium, carefully dried over phosphorus pentoxide, and 10 g of mercuric trifluoroacetate were mixed and placed in a glass tube, about 20 mm in diameter and 200 mm in length, sealed at one end. The reaction mixture was gradually heated in an open flame, and the reaction products were collected in a trap cooled with liquid air. After the reaction was finished, the contents of the trap were slowly heated to room temperature. The liquid obtained (3.2 g) was washed with an equal volume of ice water, dried with sodium sulfate and distilled. There was obtained 1.1 g (16%) of hexafluorodimethyl diselenide.

Under similar conditions, hexafluorodimethyl diselenide was obtained in 28% yield from silver trifluoroacetate and selenium.

B.p. 70°, n_D 1.4035, d^{18}_4 2.2031.

Found %: F 39.01, 38.87; Se 52.98, 53.25. $C_2F_6Se_2$. Calculated %: F 38.51; Se 53.40.

Trifluoromethylselenium chloride. To 3.2 g of hexafluorodimethyl diselenide, cooled to the point of incipient crystallization, was added 0.75 g of chlorine in small portions with constant stirring. The reaction was carried out at the lowest possible temperature, without complete solidification of the reaction mixture. As trifluoromethylselenium chloride was formed, the liquid became rose-colored and then deep-red, and an inappreciable yellow precipitate settled to the bottom of the flask. On completion of the reaction, the mixture was heated to room temperature and left for several hours. On distillation, 3.4 g (36%) of trifluoromethylselenium chloride was obtained.

B.p. 31°, $n^{14}D$ 1.3930, d^{14}_4 1.9899.

Found %: F 31.29, 31.09; Cl 19.43, 19.52; Se 42.82, 42.79. CF_3ClSe. Calculated %: F 31.06; Cl 19.35; Se 43.05.

Trifluoromethylselenium bromide. To 2.7 g of hexafluorodimethyl diselenide, 1.46 g of bromine was added dropwise with cooling in ice water. As trifluoromethylselenium bromide formed, the liquid became rose-colored, and then deep-red. Within 15 minutes after the calculated quantity of bromine was added, the liquid was distilled. There was obtained 3.5 g (84%) of trifluoromethylselenium bromide.

B.p. 57°, n_D 1.4270, d^{24}_4 2.3567.

Found %: F 24.93, 24.80; Br 34.89, 34.94; Se 34.59, 34.73; C 5.86. CF_3BrSe. Calculated %: F 25.0; Br 35.09; Se 34.65; C 5.26.

Trifluoromethyl selenocyanate. To a solution of 4.0 g of trifluoromethylselenium chloride in 8 ml of ether, a solution of 1.55 g of potassium cyanide in 1.5 ml of water was added in small portions with stirring and cooling (temperature not over 5°). During the reaction, the color of the solution changed from deep-red to light-yellow, and potassium chloride was precipitated.

After the reaction was finished, the liquid was filtered, dried with sodium sulfate, and distilled. There was obtained 3.77 g (61%) of trifluoromethyl selenocyanate.

B.p. 80°, $n^{22}D$ 1.3875, d^{22}_4 1.7912.

Found %: F 45.33, 45.55; Se 32.10, 32.58. C_2F_3NSe. Calculated %: F 45.40; Se 32.76.

Trifluoromethyl-β-chloroethyl selenide. Into a test tube provided with inlet and outlet tubes was put 1.7 g of trifluoromethylselenium chloride. The inlet tube was connected to a gas reservoir filled with ethylene, the latter was blown through the apparatus until the air was completely removed, and the outlet tube was closed. The absorption of the calculated quantity of ethylene took several minutes, and the entire reaction took place with the outlet-tube stopcock closed.

On distillation, trifluoromethyl-β-chloroethyl selenide was obtained in quantitative yield.

B.p. 110°, $n^{14}D$ 1.4355, d^{14}_4 1.6910.

Found %: F 27.50; Cl 16.66; Se 37.29; C 17.08; H 2.01. $C_3H_4F_3ClSe$. Calculated %: F 27.30; Cl 16.53; Se 37.40; C 17.42; H 2.18.

Trifluoromethyl acetonyl selenide. To 0.995 g of acetone, 3.30 g of trifluoromethylselenium chloride was added dropwise with cooling in ice water, and the mixture was left at room temperature until the evolution of hydrogen chloride ceased. It was then washed with water, and the oil was drawn off, dried with sodium sulfate, and distilled. There was obtained 1.8 g of trifluoromethyl acetonyl selenide.

B.p. 119°, $n^{16}D$ 1.4170, d^{16}_4 1.7502.

Found %: F 27.76, 27.83; Se 38.29, 38.43; C 23.34, 23.41; H 2.68, 2.53. $C_4H_5OF_3Se$. Calculated %: F 27.81; Se 38.54; C 23.41; H 2.44.

SUMMARY

1. A new method of preparing hexafluorodimethyl diselenide from trifluoroacetic acid salts and elementary selenium is described.

2. The following new organofluorine compounds of selenium have been prepared: trifluoromethylselenium bromide, trifluoromethyl selenocyanate, trifluoromethyl-β-chloroethyl selenide, and trifluoromethyl acetonyl selenide.

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INVESTIGATIONS IN THE FIELD OF QUINONES

XXVI. CONDENSATION OF p-QUINONES WITH ETHYL FUROYLACETATE, ACETYLACETONE AND DIBENZOYLMETHANE

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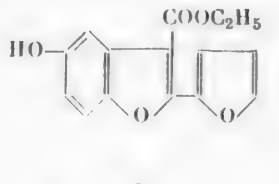
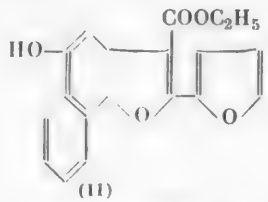
The interaction of p-quinones with ethyl acetoacetate and its analogs has already been studied in detail in our works [1-13]. This reaction, which occurs in the presence of zinc chloride, leads to derivatives of benzofuran, benzodifuran and naphthofuran. We have now investigated the reactions of p-benzoquinone and α-naphthoquinone with ethyl furoylacetate,* acetylacetone and dibenzoylmethane. The condensation of p-benzoquinone and α-naphthoquinone with ethyl furoylacetate, which takes place similarly to the interaction of these quinones with other α-ketoacid esters, leads to the formation of 2-furyl-3-carbethoxy-5-hydroxybenzofuran (I), a derivative of benzodifuran, and 2-furyl-3-carbethoxy-5-hydroxynaphthofuran (II). The two structural formulas (III) and (IV) may be surmised for the obtained benzodifuran derivative.



(I)



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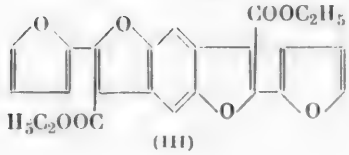

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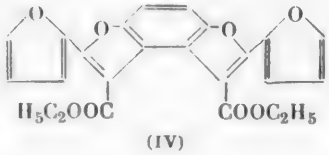
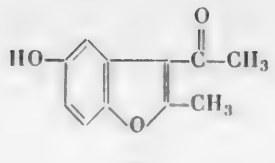


(IV)

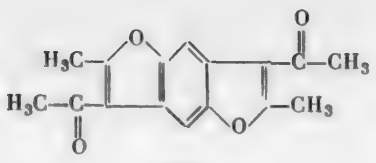
The reaction of p-benzoquinone with acetylacetone in pyridine was first observed by Ionescu [15], but he proposed an incorrect structural formula for the compound obtained. After this, Bernatek [16-18] showed that 2-methyl-3-acetyl-5-hydroxybenzofuran (V) and 2,6-dimethyl-3,7-diacetylbenzo-(1,2-b; 4,5-b')-difuran (VI) are formed along with other products in the course of this reaction. Recently, Bernatek [19] published a paper in which the interaction of p-benzoquinone and α-naphthoquinone with analogs of ethyl acetoacetate in the presence of zinc chloride is described. However, this article, which was printed at the end of 1956, merely repeated the results of our investigations of 1954 on this matter [2, 4], which were published before the Bernatek article appeared.

In the present work, by studying the reactions of p-benzoquinone and α-naphthoquinone with acetylacetone in the presence of zinc chloride, we found the reaction conditions under which 2-methyl-3-acetyl-5-hydroxybenzofuran (V) and 2-methyl-3-acetyl-5-hydroxynaphthofuran (VII) are obtained in 60-65% yield.

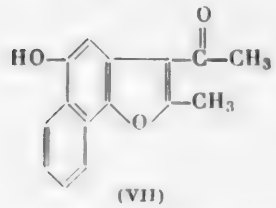
*Ethyl furoylacetate was prepared by a method described in the literature [14].



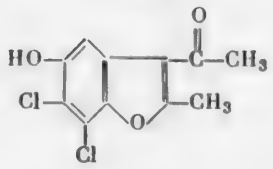
(V)



(VI)



(VII)

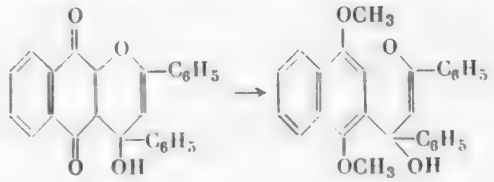


(VIII)

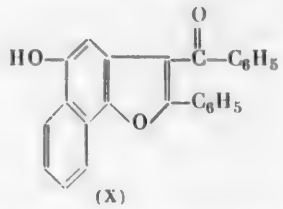
Relatively high yields of these compounds could be obtained only by gradual addition of the quinones to the reaction mixture. The reaction must be carried out in this order, as was stated earlier [3, 5, 6], because when the quinones are gradually added to the mixture of the other components, collateral oxidation-reduction processes are almost completely excluded.

Some substituted benzofurans apparently can be conveniently prepared by the reaction of p-quinones and acetylacetoneimine. For instance, 2-methyl-3-acetyl-5-hydroxy-6,7-dichlorobenzofuran (VIII) is obtained by the condensation of 2,3-dichloro-p-benzoquinone with acetylacetoneimine in 90% yield.

The reaction of α-naphthoquinone with dibenzoylmethane led to unexpected results. The main product of this reaction proved to be the adduct (IX) of α-naphthoquinone with the enol form of dibenzoylmethane, whereas 2-phenyl-3-benzoyl-5-hydroxynaphthofuran (X) was formed only in insignificant yield. On methylation with dimethyl sulfate in an alkaline medium, adduct (IX) was converted to a derivative of benzochromenol (XI).



(IX) (XI)



(X)

The series of compounds synthesized in the present work was characterized by preparing derivatives.

EXPERIMENTAL

1. Condensation of ethyl furoylacetate with p-benzoquinone. To a solution of 20.5 g of zinc chloride in 45 ml of anhydrous alcohol was added 27.3 g of ethyl furoylacetate, and then 10.8 g of p-benzoquinone; in this case, the reaction solution warmed up and darkened. It was then heated in an air bath for one hour at 100-110°. The crystals which separated after cooling the solution was filtered out, washed in the filter with alcohol, and recrystallized from dioxane. Yield of the benzodifuran derivative, 0.6 g; m.p. 254-255°.

Found %: C 66.67, 66.53; H 4.63, 4.49. $C_{24}H_{18}O_8$. Calculated %: C 66.36; H 4.18.

The mother liquor was left for seven days; the crystals which separated were filtered out and washed with water and alcohol.

Yield of (I), 4 g; m.p. 155-156° (from 50% acetic acid).

Found %: C 66.15, 66.32; H 4.64, 4.75. $C_{15}H_{12}O_5$. Calculated %: C 66.17; H 4.44.

2. Preparation of 2-furyl-3-carbethoxy-5-methoxybenzofuran (XII). A 1.45-g quantity of (I) was dissolved in 10 ml of dioxane. To the solution obtained was added 5.2 ml of 2 N sodium hydroxide and then 1 ml of dimethyl sulfate. The reaction solution was shaken for 50 minutes and diluted with water, and the precipitate formed was filtered out and washed with water. Yield of (XII), 1.3 g; m.p. 65-65.5° (from methanol).

Found %: C 67.60, 67.50; H 5.15, 5.13. $C_{16}H_{14}O_5$. Calculated %: C 67.12; H 4.93.

3. Condensation of ethyl furoylacetate with α-naphthoquinone. The reaction was carried out under the conditions of Experiment 1. For the reaction, 21.5 g of ethyl furoylacetate, 17 g of α-naphthoquinone, 16.1 g of zinc chloride, and 35 ml of anhydrous alcohol were taken. The reaction mixture was heated for 1.5 hours at 100°. The precipitate formed during the reaction was filtered out and washed with water and alcohol. Yield of (II), 17.6 g; m.p. 215-216° (from dichloroethane).

Found %: C 71.27, 71.43; H 4.62, 4.56. $C_{19}H_{14}O_5$. Calculated %: C 70.81; H 4.35.

4. Preparation of 2-furyl-3-carbethoxy-5-methoxynaphthofuran (XIII). For the experiment, 3.23 g of (II), 10 ml of 2 N sodium hydroxide, 20 ml of dioxane, and 2 ml of dimethyl sulfate were taken. The reaction was carried out under the conditions of Experiment 2. Yield of (XIII), 3.4 g; m.p. 118-119° (from alcohol).

Found %: C 71.56, 71.40; H 5.00, 4.90. $C_{20}H_{16}O_5$. Calculated %: C 71.42; H 4.80.

5. Condensation of acetylacetone with p-benzoquinone. For the experiment, 20 g of acetylacetone, 10.8 g of p-benzoquinone, 16.3 g of zinc chloride, and 20 ml of anhydrous alcohol were taken. The reaction was carried out under the conditions of Experiment 1. After the reaction was finished, the reaction mixture was cooled with ice water, and the crystalline precipitate formed was filtered out, washed with ether and dried. There was obtained 4.1 g of crystals with m.p. 207-212°. They were boiled with 450 ml of a mixture of acetone and alcohol (1:1). The undissolved crystals were filtered out and recrystallized from glacial acetic acid. Yield of (VI), 1 g; m.p. 248-249°.

Found %: C 70.73, 70.82; H 5.25, 5.15. $C_{16}H_{14}O_4$. Calculated %: C 71.10; H 5.22.

On cooling the filtrate with ice, the substance, dissolved in the alcohol-acetone mixture, precipitated. It was filtered out and recrystallized from alcohol. Yield of (V), 2.5 g; m.p. 234°.

Found %: C 69.60, 69.71; H 5.20, 5.36. $C_{11}H_{10}O_3$. Calculated %: C 69.46; H 5.30.

6. Condensation of acetylacetone with p-benzoquinone in an extractor. For the reaction, 40 g of acetylacetone, 21.6 g of p-benzoquinone, 32.6 g of zinc chloride, 64 ml of anhydrous alcohol, and 40 ml of absolute ether were taken. The p-benzoquinone was put into the thimble of the extractor,* and the rest of the substances into the extractor flask, the zinc chloride being dissolved beforehand in the alcohol. The p-benzoquinone was extracted into the extractor flask for six hours at 110-120° (air-bath temperature). The reaction mass was cooled, and the crystals which separated were filtered out and washed with water and alcohol. Yield of (V), 24.7 g; m.p. 234-235° (from an alcohol-acetone mixture, 1:1). A mixture test with the compound (V), obtained in the preceding experiment, showed no melting-point depression.

7. Condensation of acetylacetone with α-naphthoquinone. A 4.1 g quantity of zinc chloride was dissolved in 4 ml of anhydrous alcohol. To the solution obtained was added 10 ml of acetylacetone; then 4.74 g of α-naphthoquinone was added during 15 minutes with stirring, the mixture being heated to 80-90°. The reaction mixture was heated for 45 minutes at 100°. The precipitate formed was filtered out, washed with ether, and recrystallized from alcohol. Yield of (VII), 4.8 g; m.p. 246-248°.

Found %: C 75.28, 75.13; H 5.19, 5.24. $C_{15}H_{12}O_3$. Calculated %: C 74.99; H 5.03.

8. Condensation of 2,3-dichloro-p-benzoquinone with acetylacetoneimine. A solution of 8 g of 2,3-dichloro-p-benzoquinone in 10 ml of chloroform and one of 4.5 g of acetylacetoneimine in 15 ml of chloroform were mixed at room temperature. Marked warming and effervescence of the solvent were observed; in this case, a precipitate formed. To complete the reaction, the reaction mixture was heated for 45 minutes in a water bath; the crystals which had separated were filtered out and washed with ether. Yield of (VIII), 10.5 g; m.p. 256-257° (from aqueous dioxane). A mixture test of this substance with (VIII), prepared by condensation of acetylacetone with 2,3-dichloro-p-benzoquinone [13], showed no melting-point depression.

9. Condensation of dibenzoylmethane with α-naphthoquinone. For the experiment, 28.5 g of dibenzoylmethane, 20.1 g of α-naphthoquinone, 27 g of zinc chloride, and 54 ml of anhydrous alcohol were taken. The reaction mixture was heated in an air bath, a temperature of 75-78° being maintained inside the flask; the entire

*In the reaction the extractor was used without a siphon.

mass crystallized within 30 minutes; after cooling, the crystals were filtered out and washed with water and a little alcohol. Yield of crystalline products, 40 g. Two different products were obtained by fractional recrystallization from alcohol: 15 g of alcohol-soluble adduct (IX), m.p. 174-175° (from dichloroethane), in the form of white, acicular crystals, and 1.5 g of naphthofuran derivative (X), which is poorly soluble in alcohol; bright-yellow crystals with m.p. 224-225° (from alcohol).

Substance (IX). Found %: C 78.80, 78.59; H 4.85, 4.73. $C_{25}H_{18}O_4$. Calculated %: C 78.52; H 4.74.

Substance (X). Found %: C 82.55, 82.61; H 4.50, 4.54. $C_{25}H_{16}O_3$. Calculated %: C 82.40; H 4.43.

10. Methylation of adduct (IX). A 7.8-g quantity of adduct (IX) was dissolved in 20 ml of 2 N sodium hydroxide solution and 10 ml of dioxane; the solution turned deep-blue. To the solution obtained was added 5 ml of dimethyl sulfate. A reaction began immediately with evolution of heat. The reaction solution was cooled and shaken for 30 minutes at room temperature. The reaction mass was diluted with water and the precipitate was filtered out, washed with water and dried. Yield of (XI), 7.5 g; m.p. 160-160.5° (from alcohol).

Found %: C 79.28, 79.06; H 5.45, 5.41. $C_{27}H_{22}O_4$. Calculated %: C 79.00; H 5.40.

SUMMARY

1. The condensation of p-benzoquinone and α-naphthoquinone with ethyl furoylacetate and acetylacetone, α-naphthoquinone with dibenzoylmethane, and 2,3-dichloro-p-benzoquinone with acetylacetoneimine has been studied.

2. It has been established that the results of these reactions depend to a considerable degree on the conditions under which they are carried out, and also on the nature of the initial substances entering into the reaction.

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NEW AROMATIC HOMOLOGS OF TAURINE

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Not so long ago, it was shown in our laboratory [1] that homologs of taurine could be prepared by the reductive amination of β-ketosulfonic acids, which are readily available today [2]. Using the proposed scheme of synthesis, we prepared a series of new aromatic homologs of taurine-substituted β-phenyltaurines. The original aliphatic-aromatic ketones, prepared by the Friedel-Crafts condensation of the corresponding compounds of the benzene series with acetyl chloride [3], were converted by means of sulfur trioxide-dioxane complex to β-ketosulfonic acids. The latter have not been described previously in the literature, and for this reason the constants for their ammonium and S-benzylthiuronium salts are given in Table 1.

TABLE 1

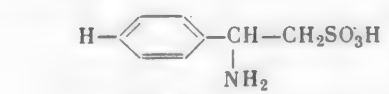
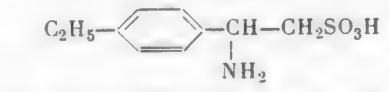
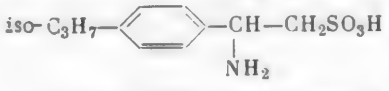
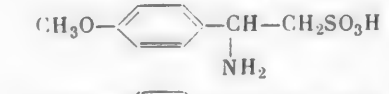
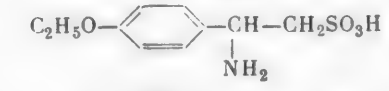
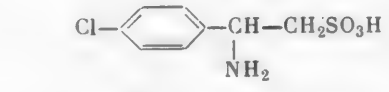
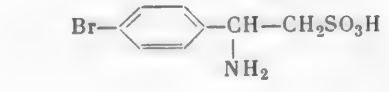
Aliphatic-Aromatic β-Ketosulfonic Acids

Ketosulfonic acid	Yield (%)	Melting point		S-Benzylthiuronium salt		
		of the free acid	of the NH_4 salts	melting point	% N	
					found	calc.
$C_6H_5—COCH_2SO_3H$	93.4	71—74°	207—209°	138—138.5°	7.53, 7.57	7.64
$C_2H_5—C_6H_4COCH_2SO_3H$	79.2		221—224	176	7.17, 6.97	7.10
iso-$C_3H_7—C_6H_4COCH_2SO_3H$	87.2		211—213	163.5	6.45, 6.55	6.85
$CH_3O—C_6H_4COCH_2SO_3H$	84.0	113—115	219—220	164—165	6.96, 7.06	7.07
$C_2H_5O—C_6H_4COCH_2SO_3H$	80.4		219—221	170.5—171	5.61, 5.46	5.36
$Cl—C_6H_4COCH_2SO_3H$	55.6	109—111	244—245	216—217	6.97, 6.83	6.96
$Br—C_6H_4COCH_2SO_3H$	58.2		247—249	221.5—222	6.17, 6.34	6.28

The ammonium salts of the β-ketosulfonic acids were reductively aminated. As reagents formamide (method A), a mixture of 85% formic acid,and ammonium carbonate (method B), and also a mixture of urea and anhydrous formic acid (method C) were used. In the case of the preparation of β-phenyltaurine from ammonium ω-acetophenonesulfonate it was shown that better yields are obtained when the ammonium carbonate-85% formic acid mixture is used. In order to avoid possible hydrolysis of the sulfo group at the beginning of the reaction, while the medium was acid owing to the excess of formic acid, we drove off the water by heating the mixture to 185° in a Wurtz flask connected to a descending condenser. After the resulting mixture of formamide and ammonium formate was cooled, the ammonium β-ketosulfonate was added, and the mixture was heated to 180-185° for six hours. The reaction began at 120-125° and was most vigorous at 170-180°. The evolution of hydrogen sulfide was observed, which indicates that the sulfo group was affected. In order to find out whether the sulfo group affected in the reaction is that of the original β-ketosulfonic acid or that of the aminosulfonic acid formed, a control experiment was performed with the ammonium salt of N-formyl-β-phenyltaurine; after the latter was heated for six hours to 185° with a mixture of formamide and ammonium formate and the reaction mixture hydrolyzed with hydrochloric acid, 98.5% of the β-phenyltaurine taken was recovered. During the reaction the odor of hydrogen sulfide was not detected, and no precipitate was observed on passing the evolved gases into lead

TABLE 2

Aromatic Homologs of Taurine

Taurine	Method	Yield (%)	M.p.	% C		% H		% N	
				found	calc.	found	calc.	found	calc.
	A B C	67.2 76.6 55.0	347—349°	—	—	—	—	—	—
	C	70.0	360 (does not melt)	52.41, 52.45	52.36	6.74, 6.89	6.56	6.26, 6.44	6.13
	C	83.3	360 (does not melt)	—	—	—	—	5.54	5.76
	C	54.0	285—286	—	—	—	—	6.09, 6.16	6.05
	A C	58.0 51.0	287—287.5 286—287	—	—	—	—	5.90, 5.83	5.71
	C	Quantitative	360 (does not melt)	41.36, 41.34	40.96	4.52, 4.43	4.37	—	—
	C	95.7	360 (does not melt)	34.81, 34.70	34.39	3.41, 3.47	3.54	—	—

acetate solution. All this indicates that the sulfo group of the aminosulfonic acid formed in the course of the Leuckart reaction is not affected under the reaction conditions.

Quantitative yields of certain β-phenyltaurine derivatives (p-chloro- and p-bromo-β-phenyltaurines) were obtained on reaction of the corresponding β-ketosulfonic acids with a mixture of urea and anhydrous formic acid. Data on the taurines obtained are given in Table 2.

EXPERIMENTAL

Aliphatic-aromatic β-ketosulfonic acids. The original aliphatic-aromatic β-ketosulfonic acids were prepared by sulfonating the corresponding substituted acetophenones with sulfur trioxide-dioxane complex, according to the method described earlier [2]. All sulfonic acids were identified in the form of the ammonium and S-benzylthiuronium salts (see Table 1). Certain sulfonic acids were isolated from dichloroethane solution in the free state after sulfonation.

Syntheses of Taurines

Method A. Preparation of β-phenyltaurine by the reaction of ammonium ω-acetophenonesulfonate with formamide. A mixture of 10.9 g of ammonium ω-acetophenonesulfonate and 9 g of formamide was heated to 185° for six hours. When the reaction was finished, the mixture was boiled with 50 ml of hydrochloric acid (1:1). The precipitate formed was filtered out and dried. Yield 6.74 g (67.2%).

Method B. Preparation of β-phenyltaurine by the reaction of ammonium ω-acetophenonesulfonate with a mixture of ammonium carbonate and formic acid. A mixture of 10.8 g of 85% formic acid and 5.5 g of ammonium carbonate was heated in a Wurtz flask connected to a descending condenser. To the homogeneous mass obtained, after cooling to 60-70°, 10.9 g of ammonium ω-acetophenonesulfonate was added. The mixture was heated for six hours at a temperature not over 180-185°. The reaction began at 125-130° and was particularly vigorous at 165-170°. The evolution of hydrogen sulfide was observed (odor and the appearance of a dark precipitate on passing the evolved gases into lead acetate solution). When the reaction was finished, the mixture was hydrolyzed with hydrochloric acid. Yield of β-phenyltaurine, 7.7 g (76.6%). M.p. 347-349° (decomp.) after two recrystallizations from hot water.

Method C. Preparation of β-phenyltaurine by the reaction of ammonium ω-acetophenonesulfonate with a mixture of urea and anhydrous formic acid. A mixture of 6 g of urea and 9.5 ml of anhydrous formic acid was heated in a round-bottomed flask, provided with a reflux condenser, until a homogeneous mass was formed, after which 10.9 g of ammonium ω-acetophenonesulfonate was added to the flask, and the mixture was heated for six hours at 140-160° (thermometer in the mass). After hydrolysis of the reaction mixture with hydrochloric acid (1:1), 5.5 g of β-phenyltaurine was obtained (yield 55.0%).

All the rest of the aromatic homologs of taurine were prepared by the methods described above. See data on them in Table 2.

SUMMARY

1. Six new members of the β-ketosulfonic acid series have been prepared by treatment of substituted acetophenones with sulfur trioxide-dioxane complex.

2. The β-ketosulfonic acids obtained have been converted to homologs of taurine by reductive amination according to Leuckart.

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STEREOCHEMICAL INVESTIGATIONS

V. OPTICALLY ACTIVE β-PHENYLTAURINE

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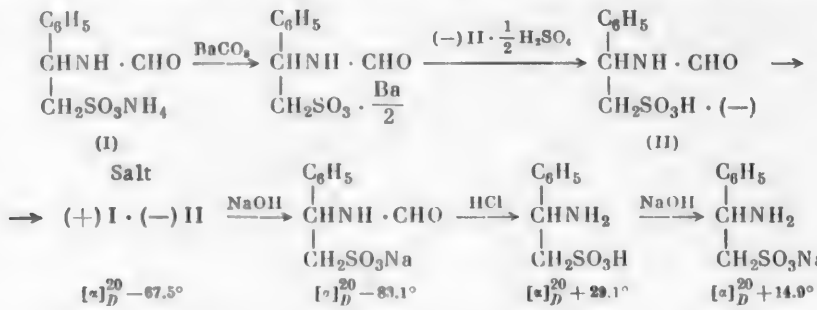
In our laboratory, not so long ago, a convenient method of synthesis of homologs of taurine from ketones, by successively sulfonating them with sulfur trioxide-dioxane complex and reductively aminating according to Leuckart, was developed [1]. Taurine homologs of the type $Ar-CHNH_2-CH_2SO_3H$, so obtained, have an asymmetric carbon atom. It was of interest to attempt to prepare them in an optically active form. Our attempt in this direction showed that β-phenyltaurine actually can be obtained in an optically active form. For this we converted the ammonium salt of N-formyl-β-phenyltaurine (I) to its barium salt which, on reaction with (−) α-phenylethylamine sulfate (II), gave diastereomeric I (−) II salts; by recrystallization of the latter from water, one of the diastereomers was isolated, and this, in turn, gave optically active β-phenyltaurine on decomposition.



It should be noted that optically active β-phenyltaurine substantially differs from racemic in the form and properties of the crystals. The racemate crystallizes in the form of white, hexagonal plates melting at 347-349°. The solubility of the racemate in water is very low. Optically active β-phenyltaurine, on the contrary, is readily soluble in hot water and separates out on cooling in the form of white, acicular crystals melting at 317-320°.

EXPERIMENTAL

The solution of β-phenylethylamine into antipodes was carried out by a somewhat modified procedure [2]. The (−) amine was isolated in this procedure by treatment with D-tartaric acid in methanol solution. From the methanolic filtrate obtained after filtering out the (−) amine D-tartrate, the optically impure (+) amine was isolated; it was dissolved in alcohol, and sufficient sulfuric acid was added to convert the excess (+) amine to the sulfate. The precipitated (+) amine sulfate was filtered out and purified by recrystallization from water.• We determined the amine content of the filtrate, containing the racemate, by titration and again treated it with D-tartaric acid, thus isolating the (+) amine. Thus, we succeeded in conducting a "cyclic process," successively separating the (−) and (+) amines.

Barium salt of N-formyl-β-phenyltaurine. The ammonium salt of N-formyl-β-phenyltaurine, which was

•$[\alpha]_D^{20}$ of the optically pure (+) sulfate, +5.7° (water, c 18).

prepared from acetophenone-ω-sulfonic acid after Leuckhart [1] was heated with freshly precipitated barium carbonate in a steam-distillation apparatus until the evolution of ammonia ceased. The excess carbonate was filtered off and the filtrate evaporated to dryness. The substance was recrystallized twice from water.

Found %: Ba 18.98, 18.64. $C_9H_{10}O_4NSBa_{1/2}$. Calculated %: Ba 19.06.

Resolution of β-phenyltaurine into antipodes. A solution of 38 g of the barium salt of N-formyltaurine and one of α-phenylethylamine sulfate, prepared by neutralizing 9.7 g of the free amine ($[\alpha]_D^{20}$ −40°) with 2 N sulfuric acid to the neutral point (methyl red indicator), were mixed. The barium sulfate precipitate was filtered out and boiled with water. The combined filtrates were evaporated to the point of incipient crystallization, and the precipitate obtained was recrystallized from water until the melting point and value of specific rotation became constant.

Results of the experiments are given in the table.

No. of recrystallization	Weight of precipitate (in g)	Melting point	Weighed portion (in g)	Weight of solution (in g)	α	$[\alpha]_D^{20}$
0	16.2	110—112°, 135—138	0.9547	8.33	—2.72	—23.7
1	8.87	139—141	0.9492	8.23	—6.73	—58.2
2	4.91	140—141	0.9103	8.75	—6.69	—65.1
3	2.83	140—141	0.9100	7.91	—7.72	—67.5

On the fourth recrystallization $[\alpha]_D^{20}$ did not change.

The salt (2.83 g) obtained after three recrystallizations was dissolved in water, and 18 ml of NaOH (0.4977 N) was added with cooling; the α-phenylethylamine which separated out was extracted with ether. The specific rotation of the resulting solution of the sodium salt of N-formyl-β-phenyltaurine amounted to −83.1°. A 23-ml quantity of concentrated hydrochloric acid was added to the solution, and the latter was evaporated in vacuo at 40-50°. The precipitate formed was filtered out and twice recrystallized from hot water. M.p. 317-320°, $[\alpha]_D^{20}$ +29.1° (water, c 17). The substance gave a qualitative reaction for sulfur and nitrogen; according to the data of elementary analysis, it was β-phenyltaurine.

Found %: C 47.61, 47.54; H 5.72, 5.65; N 6.88, 6.81. $C_8H_{11}O_3NS$. Calculated %: C 47.72; H 5.50; N 6.96.

The value of specific rotation of β-phenyltaurine varies with the pH of the medium. In 10% NaOH solution $[\alpha]_D^{20}$ +14.9°. Optically active β-phenyltaurine does not racemize on heating with alkalis. A solution of 0.3916 g of β-phenyltaurine in 10% alkali was heated in a water bath for ten hours, after which the rotation was measured: $[\alpha]_D^{20}$ +14.9°.

SUMMARY

β-Phenyltaurine has been resolved into optical antipodes through the diastereomeric salt formed by its formyl derivative with (−) α-phenylethylamine.

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ON THE INHIBITING EFFECT OF CERTAIN POLYCYCLIC AROMATIC COMPOUNDS ON THE POLYMERIZATION PROCESS

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The ability of polycyclic hydrocarbons to react with free radicals was studied in a series of investigations. Waters and his co-workers [1-3] demonstrated the moderating action of many polycyclic compounds, mainly of the anthracene series, on the process of oxidation of benzaldehyde, initiated by benzoyl peroxide. In this case, the authors were unable to find any connection between the inhibiting effect and the carcinogenic activity of the hydrocarbons. It should be noted that in biochemical systems, in which oxidation processes apparently develop with the participation of radicals with a reaction center on an oxygen atom ($HO^{\cdot}$, $RO^{\cdot}$, etc.), the relation between the structure of the hydrocarbon and its inhibiting action may be entirely different in character. In the case of radicals of the type $AO^{\cdot}$, the primary reaction tends mainly toward removal of a hydrogen atom from the hydrocarbon (formation of AOH); in the case of alkyl radicals, it tends mainly toward their addition to the inhibitor.

Kooijman and Farenhorst [4] studied the moderating action of polycyclic hydrocarbons in the processes of addition of CCl_4 to hexadecene-1 and $CBrCl_3$ to styrene, which are initiated by benzoyl peroxide, and arranged them in the order of increasing effectiveness of inhibiting action, as follows: benzene, biphenyl, anthracene, phenanthrene, naphthalene, chrysene, stilbene, pyrene, benzanthracene, dibenzanthracene, etc.; in this case, it is stated that 3,4-benzopyrene is 100,000 times as active as benzene.

Bickel and Kooijman [5] established that the 2-cyanoisopropyl (R) adds to anthracene (A) in the 9 or 10 position, forming the radical $RA^{\cdot}$ with free valences in the meso-position. The products RAAR and RAR are formed as a result of recombination reactions. The work by Beckwith and Waters [6] is devoted to the interaction of polycyclic aromatic hydrocarbons with the radical $CH_3^{\cdot}$, which is formed along with an alkoxy radical in the thermal decomposition of di-tert-butyl peroxide. The authors isolated the products formed in the interaction of anthracene with the $CH_3^{\cdot}$ radical and studied them in detail. The inhibiting action of polycyclic compounds in the process of thermal polymerization of styrene was studied in the work by Magat and Boneme [7]. The authors carried out the thermal polymerization of styrene for 200 hours at 37°. The action of benzopyrene, methylcholanthrene, 1,2,5,6-dibenzanthracene, 2-methylanthracene, phenanthrene, pyrene, and chrysene, i.e., substances having carcinogenic activity and lacking it, was investigated. It was shown that all the substances investigated inhibit the thermal polymerization of styrene regardless of their carcinogenic activity.

In the present article we give data on the ability of certain polycyclic compounds to react with the $CH_3^{\cdot}$ radical, formed in the thermal decomposition of methylphenyltriazene, and the effect of these same compounds on the thermal polymerization of styrene at 100°.

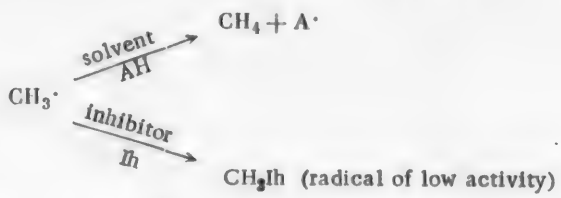
EXPERIMENTAL

1. Interaction of Polycyclic Hydrocarbons with the Methyl Radical

As a source of free methyl radicals, we used methylphenyltriazene, which thermally decomposes according to the equation

$$C_6H_5{-}N{=}N{-}NHCH_3 \rightarrow C_6H_5NH\cdot + N_2 + CH_3\cdot.$$

The methyl radical takes hydrogen from the solvent to form methane, the yield of which amounts to 55-60% of the theoretical in saturated hydrocarbons [8]. In the case of the decomposition of methylphenyltriazene in the presence of quinones and various aromatic compounds, the latter are alkylated by the methyl radical; this is accompanied by a corresponding decrease in the yield of methane. In the given case the concurrent reactions are



In work with the same solvent the activity of one compound or another, with respect to the methyl radical, may be characterized by the amount of methane.

The decomposition of methylphenyltriazene was carried out at 110° in solution in dry, purified benzine which had been distilled through an efficient column in the temperature interval 90-110°. The data obtained are given in the table.

Effect of Polycyclic Hydrocarbons on the Yield of Methane in the Decomposition of Methylphenyltriazene

Inhibitor	Concentration (in wt. %)		Molar ratio, methylphenyltriazene : inhibitor	Yield of methane* (in %)
	methylphenyltriazene in solution	inhibitor in solution		
In the absence of inhibitor	2.80	0	–	62
Biphenyl	1.86	31.9	1 : 15	59
Naphthalene	2.30	8.5	1 : 5	56
	2.30	21.6	1 : 10	51
	1.99	28.0	1 : 15	46
Phenanthrene	2.02	26.6	1 : 10	48
	1.74	36.2	1 : 15	39
Anthracene	2.70	3.6	1 : 1	40
	2.63	9.6	1 : 2.5	31
Pyrene	2.50	9.4	1 : 2.5	60
Chrysene	2.40	10.0	1 : 2.5	60
Nitrobenzene	2.64	6.7	1 : 2.5	40
Dinitrobenzene	2.60	8.28	1 : 2.5	20
	2.78	3.48	1 : 1	22
Benzoquinone	2.70	2.2	1 : 1	2
	2.60	4.2	1 : 2	0

*The listed figures are averages from two experiments.

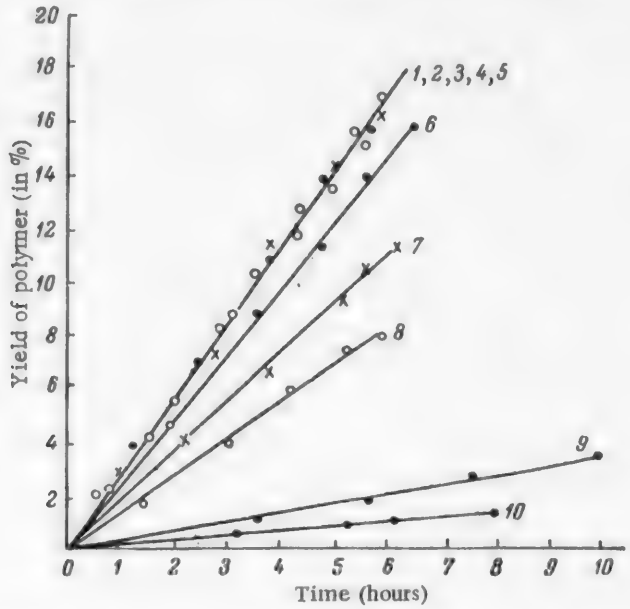
It follows from the listed data that, under the conditions of the experiment, biphenyl was only feebly active with respect to the methyl radical. Even when the molar ratio of biphenyl to methylphenyltriazene was 15:1, the yield of methane was practically unchanged. Naphthalene and phenanthrene, at the same concentration, substantially decreased the yield of methane. Thus, for a naphthalene content of 10 and 15 moles per mole of methylphenyltriazene, the yield of methane fell from 62 to 51 and 46%, respectively. A similar picture was observed for phenanthrene. Owing to their limited solubility in benzine, experiments with chrysene and pyrene were conducted only at a ratio of 2.5 moles per mole of methylphenyltriazene. The extremely low solubility of dibenzopyrene did not permit evaluation of its activity relative to the other polycyclic compounds. The most active

of the hydrocarbons, with respect to the methyl radical, was anthracene; however, its low solubility in benzene restricted the possibility of studying the dependence of the yield of methane on the anthracene concentration. When the anthracene content was 2.5 moles per mole of methylphenyltriazene, the yield of methane fell to half.

On evaluating the ability of anthracene to "capture" methyl radicals, it should be noted that under the studied conditions it occupies an intermediate position between nitrobenzene and dinitrobenzene, which are known to be relatively weak inhibitors of radical chain processes. Under similar conditions, benzoquinone practically completely suppresses the evolution of methane.

2. Inhibiting Action of Polycyclic Hydrocarbons on the Thermal Polymerization of Styrene

Since benzyl radicals are much less reactive than methyl, it could be expected that, in the thermal polymerization of styrene, only the most active inhibitors would manifest a moderating effect.



Inhibiting effect of polycyclic aromatic compounds on the thermal polymerization of styrene at 100°: 1) thermal polymerization, without inhibitor; 2) biphenyl (1 mol %); 3) naphthalene (1 mol %); 4) phenanthrene (1 mol %); 5) pyrene (1 mol %); 6) chrysene (1 mol %); 7) anthracene (1 mol %); 8) anthracene (1.5 mol %); 9) dibenzopyrene (0.5 mol. %); 10) dinitrobenzene (0.5 mol. %).

In the study of the influence of polycyclic compounds on the thermal polymerization of styrene at 100° it was shown that naphthalene, phenanthrene, pyrene, and chrysene, in concentrations up to 1 mol %, with respect to styrene, have practically no effect on the kinetics of the process. Anthracene has an appreciable moderating effect in concentrations of 1 mol % or more (see figure, 7, 8). When the anthracene concentration was 1.5 mol % with respect to styrene, the rate of the process was decreased to about half; however, its inhibiting effect was appreciably less than that of dibenzopyrene which, like anthracene, has two carbon atoms in the meso-position. The inhibiting effect of dibenzopyrene is approximately equal to that of dinitrobenzene at the same concentration (see figure, 9, 10). Here it should be noted also that both anthracene and dibenzopyrene merely decrease the rate of polymerization of styrene more or less; they do not cause an induction period to appear. This also puts them into a group with such relatively weak inhibitors as nitro- and dinitrobenzene.

The inhibiting action of anthracene in polymerization is accompanied by a corresponding decrease in the molecular weight of the polystyrene.

Experimental procedure. The decomposition of methylphenyltriazene was carried out in an ampoule provided with a reflux condenser. Into the ampoule were put a weighed portion of methylphenyltriazene (~0.2 g) and the calculated quantity of the hydrocarbon being investigated. The air was pumped out of the system, after which the ampoule was filled with purified nitrogen. This operation was repeated three times, and benzine (10 ml) was then added to the ampoule in a current of nitrogen. The ampoule was connected through the reflux condenser to a gas buret and placed in a thermostat at a temperature of 110±0.5°. After gas evolution ceased, the ampoule was flushed out, at the temperature of the experiment, with carbon dioxide through a stopcock in order to expel the evolved gas. The gas was analyzed for methane by the usual method.

The thermal polymerization of styrene was carried out at a temperature of 99±0.5° in ampoules with graduated necks, which were filled with styrene in a special apparatus under conditions which excluded the entrance of traces of air into the system [9]. The polymerization kinetics were determined dilatometrically.

SUMMARY

1. Data, characterizing the relative activity of various polycyclic, aromatic hydrocarbons with respect to the methyl radical, have been obtained.

2. Of the hydrocarbons investigated, the most effective inhibitor of the thermal polymerization of styrene is dibenzopyrene.

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SULFONATION OF β-DIKETONES

IV. 5,5-DIMETHYL-1,3-CYCLOHEXANEDIONE-2-SULFONIC ACID AND ITS SALTS

É. Yu. Gudrinietse, A. F. Ievin'sh and G. Ya. Vanag

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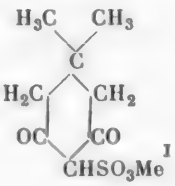
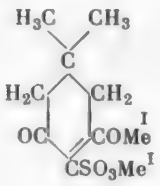
Earlier [1, 2] it was shown that β-diketones are easily sulfonated by sulfur trioxide-dioxane complex (D–SO_3). The sulfonation goes just as smoothly with 98% sulfuric acid in the presence of acetic anhydride. We succeeded in sulfonating a number of compounds by this method [3, 4]. Leaving the theory of the process itself, which will be set forth elsewhere, for the present, here we shall discuss the salts of 5,5-dimethyl-1,3-cyclohexanedione-2-sulfonic acid (dimedonsulfonic acid) in more detail. We obtained both the acid itself and two series of its salts: with one equivalent of metal (I) and with two equivalents of metal (II).



(I)



(II)

Dimedonsulfonic acid is a colorless, crystalline substance [5], less hygroscopic than indandionesulfonic acid [2]. It is readily soluble in water, alcohol, dioxane, and acetone and insoluble in ether, benzene, chloroform, dichloroethane, and carbon tetrachloride. On heating with hydrochloric acid it hydrolyzes, forming dimedon.

The ammonium, sodium, potassium, magnesium, calcium, strontium, barium, nickel, and cobalt salts containing one equivalent of the metal were prepared by saturating an aqueous solution of dimedonsulfonic acid with the corresponding chloride. The silver salt was prepared by metathesis between concentrated solutions of sodium dimedonsulfonate and silver nitrate or by saturating a solution of the acid with silver nitrate. The cadmium salt was prepared by dissolving cadmium carbonate in the sulfonic acid. All the enumerated salts, except those of nickel and cobalt, are colorless, crystalline substances, soluble in water. Their solubility in ethanol is far less, although the calcium, strontium, barium, cadmium, nickel, and cobalt salts have relatively high solubility even in alcohol. Aqueous solutions of salts with one equivalent of the metal have an acid reaction.

The dimedonsulfonates of organic bases are easily prepared by adding these bases to a solution of the sulfonic acid. The aniline, pyridine and quinoline salts, which we prepared, are colorless, crystalline substances, readily soluble in water.

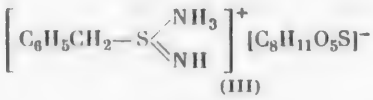
Dimedonsulfonic acid readily forms salts of the enol form (II) also. They are usually prepared by neutralizing an aqueous solution of the sulfonic acid (or the monosalt) with carbonates or hydroxides until a weakly acid (pH 6) or neutral reaction is obtained. Salts of alkali and alkaline-earth metals, as well as copper, zinc, and manganese salts, are soluble in water. Their aqueous solutions have an alkaline or neutral reaction, depending on the properties of the cation. Dimedonsulfonates with two equivalents of the metal are insoluble in ethanol. The ammonium salt of the enol form could not be prepared. Of the organic bases, a salt of the enol form could be obtained only with piperidine.

Salts of 5,5-Dimethyl-1,3-cyclohexanedione-2-sulfonic Acid

No.	Empirical formula	Calculated (%)	Found (%)	Dehydration temperature	Remarks
15	$(C_8H_{11}O_5S)_2Cd \cdot 4H_2O$	Cd 18.05, H_2O 11.57	Cd 18.10, H_2O 10.03	120°	Prismatic crystals with a slightly yellowish hue, readily soluble in water and alcohol
16	$C_8H_{10}O_5SZn \cdot 2H_2O$	Zn 20.45, H_2O 11.27	Zn 20.70, H_2O 11.33	120	Colorless needles, readily soluble in water; insoluble in alcohol
17	$C_8H_{10}O_5SPb \cdot H_2O$	Pb 46.73, H_2O 4.06	Pb 47.06, H_2O 4.20	140	Fine prisms, insoluble in water or alcohol
18	$C_8H_{10}O_5SHg$	Hg 47.90	Hg 48.05	—	Fine, yellow crystals, insoluble in alcohol
19	$C_8H_{10}O_5SMn$	Mn 20.11	Mn 19.95	—	Fine needles with a rosy hue, insoluble in alcohol
20	$(C_8H_{11}O_5S)_2Co \cdot 9H_2O$	Co 8.94, H_2O 24.58	Co 8.81, H_2O 24.23	170	Coarse, poorly developed, lamellar, rose-colored crystals, readily soluble in water and alcohol
21	$(C_8H_{11}O_5S)_2Ni \cdot 5H_2O$	Ni 9.99, H_2O 15.34	Ni 9.41, H_2O 14.77	110	Green, lamellar crystals, readily soluble in water and alcohol
22	$C_8H_{11}O_5SNH_4$	N 5.90	N 6.03	—	Long prisms. M.p. 180° (decomp.)
23	Aniline salt $C_{14}H_{19}O_5SN$	N 4.47	N 4.27	—	Long, colorless prisms; recrystallized from alcohol. M.p. 201°
24	Pyridine salt $C_{13}H_{17}O_5SN$	N 4.68	N 4.41		Hexahedral prisms. Precipitates from alcoholic solution on addition of ether. M.p. 138-140°
25	Quinoline salt $C_{17}H_{19}O_5SN$	N 4.01	N 4.08	—	Hexahedral prisms of slightly yellowish hue. Prepared similarly to the pyridine salt. M.p. 152-153°
26	Piperidine salt $C_{18}H_{23}O_5SN$	N 7.19, S 8.24	N 7.43, S 8.44	—	Lamellar crystals, readily soluble in water and alcohol. M.p. 168-170°
27	S-Benzylthiuronium salt $C_{16}H_{22}O_5S_2N_2$	N 7.27	N 7.02	—	M.p. 140-142°

No.	Empirical formula	Calculated (%)	Found (%)	Dehydration temperature	Remarks
1	$C_8H_{10}O_5SLi_2$	Li 5.98	Li 5.79		Fine, acicular crystals, difficultly soluble in alcohol
2	$C_8H_{11}O_5SNa \cdot 3H_2O$	Na 7.76, H_2O 18.24	Na 7.71, H_2O 17.98	110°	Fine plates and prisms
3	$C_8H_{10}O_5SNa_2 \cdot H_2O$	Na 16.30, H_2O 6.38	Na 16.32, H_2O 6.49	105	Fine, acicular crystals, difficultly soluble in alcohol
4	$C_8H_{11}O_5SK$	K 15.13	K 14.84	—	Plates and prisms. Decomposes at 230°
5	$C_8H_{10}O_5SK_2 \cdot 1^1/_2H_2O$	K 24.17, H_2O 8.36	K 24.01, H_2O 8.38	120	Fine needles, very soluble in water and insoluble in alcohol
6	$C_8H_{11}O_5SAg \cdot H_2O$	Ag 31.26, H_2O 5.22	Ag 31.31, H_2O 5.29	110	Rectangular plates, soluble in water and insoluble in alcohol; they decompose in the light
7	$(C_8H_{11}O_5S)_2Mg \cdot 7H_2O$	Mg 4.13, H_2O 21.41	Mg 4.23, H_2O 21.23	120	Transparent needles
8	$(C_8H_{11}O_5S)_2Ca \cdot 2H_2O$	Ca 7.79, H_2O 7.00	Ca 7.83, H_2O 7.25	120	Plates of indefinite form, soluble in water and alcohol
9	$C_8H_{10}O_5SCa \cdot 2H_2O$	Ca 13.62, H_2O 12.24	Ca 13.51, H_2O 12.27	120	Long needles, readily soluble in water and poorly in alcohol
10	$(C_8H_{11}O_5S)_2Sr \cdot 6H_2O$	Sr 13.73, H_2O 17.04	Sr 13.30, H_2O 17.07	120	Poorly developed, shiny plates, readily soluble in water and alcohol
11	$C_8H_{10}O_5SSr \cdot 2H_2O$	Sr 25.63, H_2O 10.54	Sr 25.27, H_2O 10.82	120	Lamellar crystals with nacreous luster, poorly soluble in alcohol
12	$(C_8H_{11}O_5S)_2Ba \cdot 4H_2O$	Ba 21.20, H_2O 11.12	Ba 20.70, H_2O 11.30	110	Long, fine needles, readily soluble in water and alcohol
13	$C_8H_{10}O_5SBa \cdot H_2O$	Ba 36.77, H_2O 4.82	Ba 36.60, H_2O 4.49	120	Fine, lamellar crystals, insoluble in alcohol
14	$C_8H_{10}O_5SCu$	Cu 22.55	Cu 22.46	—	Fine, green, lamellar crystals, readily soluble in water and insoluble in alcohol

Like other sulfonic acids, dimedonsulfonic acid reacts with S-benzylthiuronium chloride to form a benzylthiuronium salt (III) which crystallizes well and may be used to characterize the acid.



(III)

EXPERIMENTAL•

5,5-Dimethyl-1,3-cyclohexanedione-2-sulfonic acid. To 2.8 g of dimedon was added a mixture of 8 ml of 1,2-dichloroethane, 3 ml of acetic anhydride, and 1.3 ml of 98.5% sulfuric acid, and the whole was vigorously shaken. It was desirable to keep the temperature within the 20-40° range. The dimedon dissolved quickly, and an oily layer (sulfonic acid) appeared at the bottom of the flask. The reaction was finished within 30 minutes, and the flask was left for several hours at a temperature below 0°; the oil gradually crystallized. The crystals were filtered out, washed with ether, and dried in a vacuum desiccator. Yield 3.1 g (70.09%). M.p. 90-91°.

Found %: S 14.75. $C_8H_{12}O_5S$. Calculated %: S 14.60.

Sulfonation with sulfur trioxide-dioxane complex was carried out as indicated for the preparation of indandionesulfonic acid [2].

Salts of 5,5-dimethyl-1,3-cyclohexanedione-2-sulfonic acid. To prepare a salt with one equivalent of metal, the mass, after sulfonation, was washed twice with water (about 20 ml) in a separatory funnel and salted out from the aqueous solution obtained, with the corresponding chloride. If any free sulfonic acid remained, it was dissolved in a little water and salted out with the chloride. The precipitates were recrystallized from dilute ethanol.

To prepare salts of the enol form, an aqueous solution of the sulfonic acid (or a monosalt) was neutralized with a carbonate or hydroxide. These salts (except the lead) are relatively highly soluble in water and insoluble in alcohol. After recrystallization the lead salt was dissolved in dilute nitric acid, from which it was again precipitated on neutralizing the solution with ammonia. The enol salts of lithium, potassium, copper, and zinc, owing to their great solubility in water, crystallized only when the aqueous solutions were evaporated to a high concentration and sufficient alcohol was added. The pyridine and quinoline salts were crystallized from ether-alcohol solutions. The S-benzylthiuronium salt was prepared from sodium dimedonsulfonate and benzylthiuronium chloride in alcoholic solution.

The dimedonsulfonates prepared by us are given in the table.

SUMMARY

1. 5,5-Dimethyl-1,3-cyclohexanedione was sulfonated with sulfuric acid in the presence of acetic anhydride or with sulfur trioxide-dioxane complex to give dimedonsulfonic acid, which is easily enolized.

2. It has been found that either the sulfo group alone or the sulfo group together with the enol can take part in the formation of dimedonsulfonic acid salts. A number of salts of both types have been prepared.

3. Dimedonsulfonic acid may be characterized by means of its S-benzylthiuronium salt.

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β-HALOACROLEINS

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In the process of investigations of functional derivatives of malondialdehyde and their use in synthesis, we prepared β,β-dihalopropionaldehydes CHX_2-CH_2-CHO (I, X = Cl or Br). It was also shown that the semicarbazones and arylhydrazones of these aldehydes are easily converted to the corresponding β-haloacrolein derivatives with loss of hydrogen halide [1]. Somewhat earlier V.T. Klimko, V.A. Mikhalev and one of us established that alkyl and, correspondingly, aryl β-chlorovinyl ketones may be obtained by treatment of β,β-dichloroethyl ketones with basic agents under mild conditions [2].

Proceeding from these data, we attempted to convert β,β-dihalopropionaldehydes (I) to the corresponding β-haloacroleins CHX = CH−CH = O (II, where X = Cl or Br), which are of substantial interest for purposes of synthesis. β-Haloacroleins may be regarded as vinylogs of the hypothetical formyl halides, and are also the simplest analogs of alkyl β-chlorovinyl ketones – a class of compounds, which, as the investigations of A.N. Nesmeyanov and N.K. Kochetkov showed, opens up broad possibilities for the synthesis of aliphatic, alicyclic and heterocyclic compounds [3].

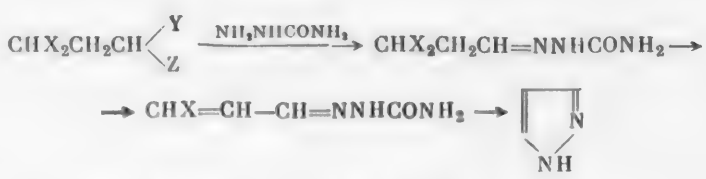
After the present investigation was completed, Italian works were published, which described the preparation of crude β-chloroacrolein through the oxidation of β-chloroallyl alcohol by manganese dioxide [4] and its reactions with hydroxylamine and hydrazine [5]. However, as the authors of these papers state, they were unable, owing to the extreme instability of β-chloroacrolein, to prepare the substance in a pure state or to determine its physicochemical constants.

We found that treatment of β,β-dihalopropionaldehydes (I) with aqueous sodium carbonate solution leads to the formation of the corresponding β-haloacrolein (II), which may be extracted from the aqueous solution with methylene chloride and, after removal of the latter, isolated in a pure state by fractionation in vacuo in a current of nitrogen. β-Haloacroleins are colorless liquids which quickly turn yellow on standing and very strongly irritate the mucous membranes of the eyes and nose; on keeping in the light at room temperature they quickly decompose with evolution of hydrogen halide; they are more stable when kept in the cold in the presence of traces of hydroquinone or in the form of solutions in an inert organic solvent.*

Of the many interesting chemical properties of β-haloacroleins, we shall deal only with their reactions with typical aldehyde-group reagents in the present article. As should have been expected, β-haloacroleins, which may be regarded as functional derivatives of malondialdehyde (monohalo derivatives of the enol form of the latter), repeat the reactions, described by us earlier, of 1,1,3,3-tetraalkoxypropanes [6] and derivatives of β,β-dihalopropionaldehydes [7, 8]; i.e., with semicarbazide or hydrazine they readily form pyrazole as the final reaction product; with arylhydrazines they form 1-arylpyrazoles as final products; with hydroxylamine, isoxazole; with guanidine, 2-aminopyrimidine, etc. The reaction goes through a stage of intermediate formation of aldehyde-group derivatives, of which the β-haloacrolein semicarbazones and arylhydrazones were isolated and characterized; on treatment with acids they were cyclized to the corresponding heterocycles. Although the oximes

*According to the data of the Italian authors [4], β-chloroacrolein may be kept for some time in the form of a solution in anhydrous alcohol; according to the data of our investigations (the results of which will be set forth in detail in another paper), β-chloroacrolein quickly and violently reacts with methanol, 1,1,3,3-tetramethoxypropane being formed along with other products.

and hydrazones of aldehydes (II) could not be isolated, they are probably also intermediate reaction products. In the case of the preparation of pyrazole the reaction sequence proposed earlier for the preparation of heterocyclic compounds from derivatives of β,β-dihalopropionaldehydes may be considered established, since we isolated the semicarbazones of the latter and demonstrated the possibility of their easy conversion to β-haloacrolein semicarbazones [1, 8].



where: X = Cl or Br, Y = OAc, OAlk or O/2, Z = Cl, Br or O/2.

On oxidation of β-haloacroleins with silver oxide, trans-β-haloacrylic acids were obtained.

EXPERIMENTAL

β-Chloroacrolein. A mixture of 13.1 g of 1,1,3-trichloro-3-methoxypropane [7] and 100 ml of water was shaken for three hours, the aqueous solution was separated from the small (less than 1 ml) oil layer, 10 g of anhydrous sodium carbonate was gradually added to the solution, and the latter was heated for ten minutes at a bath temperature of 35-40°, saturated with sodium chloride, and subjected to repeated extraction with methylene chloride. A little hydroquinone was added to the extracts as stabilizer, and they were dried with sodium sulfate; the methylene chloride was evaporated in vacuo at room temperature, and the residue was fractionated in a current of nitrogen. There was obtained 2.1 g (31%) of a fraction with b.p. 42-47.5° (60 mm), $n^{20}D$ 1.4820. The substance was redistilled for analysis.

B.p. 42-43.5° (60 mm), $n^{20}D$ 1.4810, d^{20}_4 1.1921, MR_D 20.10; calc. 20.45.

Found %: Cl 38.98, 39.05. C_3H_3OCl. Calculated %: Cl 39.18.

β-Chloroacrolein is a colorless liquid with a very sharp odor, which strongly irritates the mucous membranes of the eyes and nose and is slightly soluble in water and readily soluble in ether, benzene, and chloroform. It is unstable, and it quickly changes if it is kept at room temperature; however, it keeps for several days in the cold in the presence of hydroquinone and is even more stable in the form of a solution in an inert organic solvent.

Reaction of β-chloroacrolein with semicarbazide. The semicarbazone was prepared by mixing the components in a water-alcohol medium. M.p. 133-134° (decomp.) (from aqueous alcohol); it corresponds in its properties to the substance obtained earlier by conversion of β,β-dichloropropionaldehyde semicarbazone [1].

Found %: Cl 23.98, 23.91; N 28.13, 28.24. $C_4H_6ON_3Cl$. Calculated %: Cl 24.02; N 28.34.

Pyrazole. A mixture of 0.3 g of β-chloroacrolein semicarbazone and 3 ml of 20% hydrochloride acid solution was boiled for one hour, cooled, made alkaline with 25% sodium hydroxide solution, and extracted several times with ether. The ether extracts were shaken with charcoal and dried with potash; after evaporation of the ether there was obtained 0.07 g of pyrazole with m.p. 65.5-66.5°, which gave no melting point depression when mixed with a sample obtained by another method [6].*

Reaction of β-chloroacrolein with hydrazine. To an emulsion of 0.5 g of β-chloroacrolein in 5 ml of water was added a solution of 0.5 g of hydrazine hydrate in 2 ml of 50% alcohol; almost at once a pasty, reddish precipitate formed, which, when the mixture had stood for 30 hours at room temperature, was completely dissolved. The light-yellow solution was made alkaline and extracted several times with ether. The ether extract was treated with charcoal and dried with potash, and the ether was evaporated; the residue crystallized completely; weight, 0.3 g; m.p. 65-66°; it showed no melting point depression when mixed with a sample of pyrazole prepared by the method described above.

Reaction of β-chloroacrolein with p-nitrophenylhydrazine. The p-nitrophenylhydrazone was obtained by

*The same results were obtained when the semicarbazone was treated with a 25% acetic acid solution for 3 hours.

mixing the components in an aqueous medium. On determination of the melting point after recrystallization from aqueous alcohol, the substance began to decompose at 100-103° and melted with decomposition at 154°.

Found %: N 18.38, 18.31. $C_9H_8O_2N_3Cl$. Calculated %: N 18.63.

1-(p-Nitrophenyl)-pyrazole. A mixture of 0.3 g of the p-nitrophenylhydrazone, 12 ml of alcohol, and 6 ml of dilute hydrochloric acid (1:1) was boiled for two hours, the clear solution was treated with activated charcoal, and the crystals which separated were filtered out. There was obtained 0.15 g of 1-(p-nitrophenyl)-pyrazole, m.p. 169-170°. According to literature data [9], 1-(p-nitrophenyl)-pyrazole has m.p. 169.5-170°.

Reaction of β-chloroacrolein with 2,4-dinitrophenylhydrazine. The 2,4-dinitrophenylhydrazone was obtained in an alcoholic medium on addition of concentrated hydrochloric acid. Golden needles with m.p. 187-188° (decomp.) (from alcohol).

Found %: Cl 13.11, 13.14; N 20.41, 20.46. $C_9H_7O_4N_4Cl$. Calculated %: Cl 13.10; N 20.74.

1-(2',4'-Dinitrophenyl)-pyrazole. A mixture of 0.1 g of the 2,4-dinitrophenylhydrazone, 10 ml of ethyl alcohol, and 0.5 ml of concentrated hydrochloric acid was boiled for one-half hour; the light-yellow solution obtained was poured into five times its volume of water. After standing overnight, the well-formed crystals were filtered out; m.p. 107.5-108°, weight 0.05 g. After recrystallization from aqueous alcohol (with charcoal), colorless crystals with m.p. 108-108.5° were obtained. According to literature data [10], 1-(2',4'-dinitrophenyl)-pyrazole has m.p. 107-109°.

Reaction of β-chloroacrolein with hydroxylamine. To an emulsion of 1 g of β-chloroacrolein and 5 ml of water was added a solution of 0.7 g of hydroxylamine hydrochloride in 8 ml of water. The mixture obtained was left for 30 hours at room temperature, after which it was shaken with charcoal and the clarified solution mixed with saturated cadmium chloride solution. The double salt of isoxazole and cadmium chloride, which precipitated in the amount of 1.6 g (60%), was decomposed for analysis by boiling with water, and saturated cadmium chloride solution was added to the distillate. There was obtained 1.3 g of the double salt.

Found %: N 5.55, 5.53. $C_3H_3ON \cdot CdCl_2$. Calculated %: N 5.54.

Reaction of β-chloroacrolein with guanidine. To a solution of 1 g of guanidine hydrochloride in 7 ml of 40% ethyl alcohol and 2 ml of concentrated hydrochloric acid, 0.9 g of β-chloroacrolein was added dropwise with stirring. The mixture was left for 24 hours and then evaporated to a small volume, an excess of 40% sodium hydroxide solution was added, and the mass obtained was dried over phosphorus pentoxide and extracted with hot benzene. After evaporation of the benzene there was obtained 0.75 g (80%) of 2-aminopyrimidine which gave no melting point depression with a sample prepared in another way [6].

Oxidation of β-chloroacrolein to trans-β-chloroacrylic acid. To a solution of 6 g of silver nitrate in 120 ml of water was added 10 g of 25% sodium hydroxide solution, and the precipitated silver oxide was almost completely dissolved in aqueous ammonia solution. To the suspension obtained, a solution of 0.5 g of β-chloroacrolein in 20 ml of water was gradually added. A silver mirror formed almost at once. When the mixture had stood for three days at room temperature, the precipitate was filtered off, the filtrate was evaporated to a small volume, acidified with hydrochloric acid, and extracted with ether, and the ether extracts were dried with anhydrous sodium sulfate. After evaporation of the ether the residue crystallized completely. There was obtained 0.45 g of trans-β-chloroacrylic acid which, after two recrystallizations from petroleum ether (b.p. 35-55°), had m.p. 83.5-84.5°. According to literature data [11], trans-β-chloroacrylic acid has m.p. 85°.

β-Bromoacrolein. This was prepared, similarly to β-chloroacrolein (see above), from 12.05 g of 1,1-dibromo-3-chloro-3-methoxypropane [7]. Yield 1.8 g (30%).

B.p. 52-54° (34.5-35 mm), $n^{20}D$ 1.5440, d^{20}_4 1.7360, MR_D 24.40; calc. 23.43.

Found %: Br 59.62, 59.55. C_3H_3OBr. Calculated %: Br 59.21.

Semicarbazone: m.p. 138.5-139° (decomp.) (from aqueous alcohol).*

*Let us use this case to correct an error made in our earlier work [8], where the substance with m.p. 135-137° (decomp.), obtained by heating β,β-dibromopropionaldehyde semicarbazone in sodium acetate solution, was identified as the amide of pyrazole-1-carboxylic acid (according to literature data [12], m.p. 136.5°). Actually, this reaction leads to β-bromoacrolein semicarbazone, m.p. 138.5°, which is converted directly to pyrazole on heating with hydrochloric or acetic acid solution.

Found %: Br 41.74, 41.76. $C_4H_6ON_3Br$. Calculated %: Br 41.63.

p-Nitrophenylhydrazone: m.p. 117-118° (decomp.) (from aqueous alcohol).

Found %: Br 29.88, 30.10; N 15.61, 15.38. $C_9H_8O_2N_3Br$. Calculated %: Br 29.60; N 15.55.

2,4-Dinitrophenylhydrazone. Orange needles, m.p. 182° (decomp.) (from alcohol).

Found %: N 17.52, 17.47; Br 25.79, 25.61. $C_9H_7O_4N_4Br$. Calculated %: N 17.77; Br 25.38.

Oxidation of β-bromoacrolein to trans-β-bromoacrylic acid. β-Bromoacrylic acid was prepared, similarly to β-chloroacrylic acid (see above), by oxidation of 0.6 g of β-bromoacrolein with ammoniacal silver oxide solution. After evaporation of the ether extracts there was obtained 0.45 g of crude β-bromoacrylic acid which, after recrystallization from petroleum ether, had m.p. 113.5-114.5°. According to literature data [13], trans-β-bromoacrylic acid has m.p. 115-116°.

SUMMARY

1. β-Chloro- and β-bromoacroleins were prepared for the first time in a pure state, by splitting-off of hydrogen halide from β,β-dihalopropionaldehydes, and characterized.

2. Pyrazole, 1-substituted pyrazoles, isoxazole, and 2-aminopyrimidine were prepared by the reaction of β-haloacroleins with semicarbazide or hydrazine, substituted hydrazines, hydroxylamine, and guanidine, respectively; intermediately formed semicarbazones and substituted hydrazones of β-haloacroleins were isolated and characterized.

3. The oxidation of β-haloacroleins with silver oxide leads to trans-β-haloacrylic acids.

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SOME DERIVATIVES OF 4,5-DICHLORO-3,6-ENDOXOHEXAHYDRO-PHTHALIC ACID

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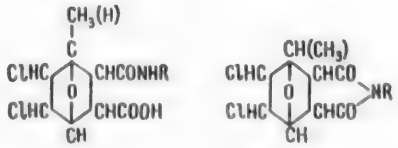
We recently showed [1] that chlorination of the anhydrides of 3,6-endoxo-1,2,3,6-tetrahydrophthalic and 3-methyl-3,6-endoxo-1,2,3,6-tetrahydrophthalic acids gave good yields of the anhydrides of 4,5-dichloro-3,6-endoxohexahydrophthalic and 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic acids. However, we did not study these compounds in more detail. There is no information in the literature on the properties of 4,5-dichloro-3,6-endoxohexahydrophthalic acids and their derivatives, although the corresponding dibromo derivatives are described in the literature and have been studied in reasonable detail [2-9] and there is a patent on their use as active defoliants [10].

In connection with a search for new active defoliants and a study of the mechanism of their action, we undertook a more detailed study of the properties and the synthesis of various derivatives of 4,5-dichloro-3,6-endoxohexahydrophthalic acid. By esterification of 4,5-dichloro-3,6-endoxohexahydrophthalic and 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic acids with various alcohols in the presence of benzenesulfonic acid, we synthesized esters of these acids which are not described in the literature and by reaction of the anhydrides with amines, we obtained the corresponding 4,5-dichloro-3,6-endoxohexahydrophthalaminic acids (I) and 4,5-dichloro-3,6-endoxohexahydrophthalimides (II). The compounds we obtained and their properties are given in the table.

Two isomers were obtained for 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic acid and the esters and amides of both isomers were prepared.



(I) (II)

Cis- and trans-4,5-dichloro-3-methyl-3,6-endoxohexahydrophthalic acids were isolated as a result of fractional crystallization of their methyl esters with subsequent acid hydrolysis of the latter. In analogy with the corresponding dibromo derivatives [11], the cis-isomer apparently has a higher melting point.

EXPERIMENTAL

1. Preparation of 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic anhydride. With vigorous stirring and cooling to −5 to +5°, 76.65 g of chlorine in 650 ml of chloroform (20% excess) was gradually added to a suspension of 162 g of 3-methyl-3,6-endoxo-1,2,3,6-tetrahydrophthalic anhydride in 65 ml of chloroform. After

the given amount of chlorine had been added, the reaction mixture was stirred for a further one hour. After separating the precipitate and evaporating the chloroform from the mother solution, we obtained 198 g of a preparation with m.p. 91-95° (88%). When the reaction was performed in more dilute chloroform solution, it was possible to isolate a small yield of 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic anhydride with m.p. 151-152°.

For resolution into isomers, the mixture of anhydrides with a melting point of 91-96° was esterified with methyl alcohol in the presence of oleum. 21 g of crude anhydride was heated with 75 ml of CH_3OH in the presence of a small amount of oleum for 34 hours in a flask with a reflux condenser. The reaction mixture was cooled and the precipitate filtered off and washed with a small amount of methyl alcohol. The m.p. was 121.5-123.5°. After recrystallization from methyl alcohol, the substance had m.p. 124-125°. The yield was 17.3 g (69.6%). According to analysis, the product obtained corresponded to the dimethyl ester of 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic acid.

The methanol mother solution was evaporated in vacuum and diluted with water and the ester extracted with benzene. The benzene extract was washed with water, sodium carbonate solution and again with water, dried over $CaCl_2$ and the solvent removed in vacuum. After removal of the benzene, the crystalline substance obtained was recrystallized from petroleum ether and methyl alcohol. The m.p. was 66-67°. The yield was 6.1 g (24.6%). The preparation obtained did not depress the melting point of the dimethyl ester, obtained from the 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic anhydride with m.p. 151-152°.

For the preparation of 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic acid, 1.4 g of the dimethyl ester with m.p. 66-67° was boiled with a mixture of 25 ml of hydrochloric acid and 25 ml of ether in a flask with a reflux condenser. After 30 minutes boiling, the solvent was removed in vacuum on a water bath. We obtained 1.09 g of 3-methyl-cis-4,5-dichloro-3,6-endoxohexahydrophthalic acid which melted at 151-152° after recrystallization from water. The acid obtained after recrystallization from water separated with two molecules of water. When dried in a vacuum desiccator over sulfuric acid, it lost 11.9% of water (11.8% for two molecules of water of crystallization) and was converted into an anhydrous preparation.

This acid was boiled with acetyl chloride for preparation of the anhydride. After recrystallization from dry ether, the anhydride obtained had m.p. 151-152° and did not depress the melting point of the anhydride of this acid described previously [1].

Under completely analogous conditions, the dimethyl ester with m.p. 124-125° was also hydrolyzed. The acid obtained from this ester melted at 151-152° and the anhydride at 113-114°. This anhydride was apparently the trans-isomer (according to the position of the halogens).

Found %: Cl 27.74, 27.79. M 257, 258. $C_9H_8O_4Cl_2$. Calculated %: Cl 28.24. M 251.

The chlorination of 3,6-endoxo-1,2,3,6-tetrahydrophthalic anhydride yielded only one isomer with m.p. 161-162°. However, the preparation of this anhydride gave as a side product a substance with m.p. 161.5-162°, which depressed the melting point of the anhydride. The structure of this compound could not be established as yet.

2. Preparation of esters of 4,5-dichloro-3,6-endoxohexahydrophthalic and 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic acids. All the esters of these acids, which are not described in the literature, were prepared by esterification of the appropriate anhydrides with alcohols in the presence of oleum or benzene-sulfonic acid. The compounds we obtained and their properties are presented in the table. The acid esters of the given acids were obtained by boiling the appropriate anhydrides with alcohols and in the preparation of the monoethyl ester of 4,5-dichloro-3,6-endoxohexahydrophthalic acid, a small amount of the substance with m.p. 161.5-162°, mentioned above, was isolated as a side product. An analogous product was isolated in the reaction of ethyl alcohol with 3-methyl-trans-4,5-dichloro-3,6-endoxohexahydrophthalic anhydride. The m.p. was 115-116°.

3. Synthesis of amides and imides of 4,5-dichloro-3,6-endoxohexahydrophthalic acids. The amides and imides of the given acids were prepared by the method described previously [1]. The compounds we prepared, which are not described in the literature, are presented in the table.

Name	Yield (%)	Temperature		Analysis for Cl (%)	
		m.p.	b.p. (pressure in mm)	found	calc.
Esters of 4,5-dichloro-3,6-endoxohexahydrophthalic acid					
Monomethyl	97	135—136°	—	26.23, 25.93	26.35
Dimethyl	93	119—120.5	—	24.74, 24.83	25.05
Monoethyl	80	150—151	—	24.85, 24.70	25.05
Diethyl	72	52—53	—	22.40, 22.28	22.79
Dipropyl*	88	—	182° (1)	20.45, 20.93	20.91
Dibutyl**	90	—	187—189 (1)	19.12, 18.84	19.31
Diisoamyl***	86	27—28	181—183 (1)	17.98, 17.50	17.94
Esters of 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic acids					
Trans-acid:					
Dimethyl	59	124—125	—	23.65, 23.93	23.87
Diethyl	63	82—83	—	22.28, 22.41	21.81
Dipropyl	91	58—59	—	19.57, 19.70	20.08
Dibutyl	58	61—62	—	18.71, 18.93	18.60
Diisoamyl	82	89.5—90.5	—	17.01, 17.18	17.32
Cis-acid:					
Dimethyl	95	66—67	—	23.87, 24.00	23.87
Diethyl	94	92—93	—	21.72, 22.08	21.81
Dipropyl	83	83.5—84.5	—	20.33, 20.10	20.08
Dibutyl	90	26—28	207—209 (2)	18.23, 18.44	18.60
Diisoamyl	90	45—46	194—196 (1)	17.46, 17.18	17.32
Amides and imides of 4,5-dichloro-3,6-endoxohexahydrophthalic acid					
N-Phenylimide	50	213—214	—	22.51, 22.55	22.72
N-α-Naphthylamide****	59	206(decomp)	—	18.47, 18.16	18.65
N-α-Naphthylimide	90	231	—	19.18, 19.24	19.58
Amides and imides of 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic acid					
Trans-					
N-Phenylamide*****	81	185(decomp)	—	4.36, 4.08	4.07(nitrogen)
N-Phenylimide	80	178.5—180.5	—	4.57, 4.50	4.30(nitrogen)
Cis-					
N-Phenylamide******	79	175(decomp)	—	4.31, 4.25	4.07(nitrogen)
N-Phenylimide	90	183.5—184.5	—	4.52, 4.51	4.30(nitrogen)

*$n^{20}D$ 1.4858.

**$n^{20}D$ 1.4830.

***$n^{20}D$ 1.4798.

****Found M 370, 366; calculated 380.

*****Found M 339, 341; calculated 344.

******Found M 340, 343; calculated 344.

SUMMARY

1. Cis- and trans-3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic anhydrides and esters, amides and imides of 3-methyl-4,5-dichloro-3,6-endoxohexahydrophthalic acids, which are not described in the literature, were synthesized.

2. A series of derivatives of 4,5-dichloro-3,6-endoxohexahydrophthalic acid, which are not described in the literature, was synthesized.

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SYNTHESIS OF SOME N-α-NAPHTHYLACETYLAMINO ACIDS

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Wood and Fontaine [1] put forward the hypothesis that in plants there exist intracellular hydrolytic enzyme systems capable of cleaving the amide bonds of N-halophenoxyacyl compounds with L- and DL-amino acids with the formation of halophenoxyalkyl carboxylic acids, which also explains the activity of the compounds. At the same time, these enzymes were assumed to be completely or partially incapable of hydrolyzing the amide bonds of compounds of halophenoxyacids with D-amino acids. To study this problem, various amino acid derivatives of 2,4-D [1], 2M-4X [2], 2,4,5-T [3], 4-chlorophenoxyacetic [4] and 2,4-dichlorophenoxy-α-propionic acids [5] were synthesized and tested on plants. The results of the test confirmed the hypothesis presented, to some extent. However, they may also be considered as confirming the fact that the activity of the compounds depends on the specificity of the structure of the molecule as a whole and on the capacity of the molecule to move through the plant [4, 5].

We proposed that in treatment with halophenoxyalkyl carboxylic acids, their amides with amino acids and products of their conversion may be formed in the plants [3]. Actually, it was recently established that 3-indolylacetyl-, 3-indolylpropionyl- and 3-indolylbutyryl-aspartic acids may be formed in plants [6-9]. Due to the importance of this problem, both theoretically and practically, a need arose for a wide investigation in this direction.

With this aim, we undertook work on the synthesis of some compounds from the N-α-naphthylacetylamino acid group. There are directions in the patent literature on the preparation of α-naphthylacetylglycine, α-naphthylacetyl-L-leucine and α-naphthylacetylsarcosine from α-naphthylacetyl chloride and the appropriate amino acids and the use of α-naphthylacetylamino acids as plant growth stimulants has been patented [10-15].

The compounds we synthesized were also prepared by the reaction of α-naphthylacetyl chloride with the appropriate amino acids in an alkaline solution.

EXPERIMENTAL

The α-naphthylacetyl chloride required for the synthesis of α-naphthylacetylamino acids was obtained from pure α-naphthylacetic acid (m.p. 132°) and thionyl chloride by the method described in [16].

Preparation of N-α-naphthylacetylamino acids. With vigorous stirring, a solution of 0.05 mole of α-naphthylacetyl chloride in benzene was added dropwise over a period of 10-15 minutes to a solution of 0.05 mole of amino acid in 0.15 mole of N sodium hydroxide solution, cooled to 0-5°. When the acid chloride had been added, the mixture was stirred for two hours at room temperature. The mixture obtained was diluted with water until the precipitate formed had dissolved. The solution was extracted three times with ether (20 ml of ether each time). The aqueous solution was acidified with hydrochloric acid (1:2) until acid to congo. The precipitate of α-naphthylacetylamino acid liberated was filtered off, washed with water, dried and recrystallized from a suitable solvent. Data on the compounds synthesized are presented in the table.

N-α-Naphthylacetylamino Acids and Their Properties

Compounds synthesized X = α-$C_{10}H_7CH_2CO$	Yield (%)	Recrystallization solvents	M.p.	$[\alpha]^{19}D$ (in pyridine)	% N		Neutralization equivalent	
					found	calc.	found	calc.
N-α-Naphthylacetylglycine $XNHCH_2COOH$	80.6	Dichloroethane and a mixture of dioxane with carbon tetrachloride	153° *	—	5.75, 6.01	5.76	245.2, 244.4	243.2
N-α-Naphthylacetylaniline $CH_3CHNHXCOOH$	76.3	A mixture of dichloroethane with dioxane and of chloroform with isopropyl alcohol	180.5—181	—	5.35, 5.36	5.44	256.3, 256.1	257.3
N-α-Naphthylacetyl-DL-serine $CH_2OHCHNHXCOOH$	73.2	Dichloroethane	124	—	5.00, 4.97	5.12	271.4, 269.9	273.3
N-α-Naphthylacetyl-DL-valine $(CH_3)_2CHCHNHXCOOH$	77.81	A mixture of benzene with dichloroethane and of chloroform with carbon tetrachloride	133	—	4.80, 4.62	4.91	281.4, 282.2	285.3
N-α-Naphthylacetyl-DL-leucine $(CH_3)_2CHCH_2CHNHXCOOH$	82.2	Benzene and a mixture of dichloroethane with carbon tetrachloride	131	—	4.85, 4.71	4.68	294.7, 293.2	299.4
N-α-Naphthylacetyl-DL-norleucine $CH_3CH_2CH_2CH_2CHNHXCOOH$	80.8	Dichloroethane and a mixture of benzene with acetone	170	—	4.70, 4.69	4.68	293.9, 295.8	299.4
N,N'-Bis-α-naphthylacetyl-L-cystine $[SCH_2CH(NHX)COOH]_2$	64.2	Dioxane	186	—75.31	4.88, 4.68	4.86	290.1, 288.5	288.3

*According to data in [10, 11, 13], the melting point of α-naphthylacetylglycine is 153-154°.

Compounds synthesized X = α-$C_{10}H_7CH_2CO$	Yield (%)	Recrystallization solvents	M. p.	$[\alpha]^{19}D$ (in pyridine)	% N		Neutralization equivalent	
					found	calc.	found	calc.
N,N'-Bis-α-naphthylacetyl-DL-cystine $[SCH_2CH(NHX)COOH]_2$	76.3	Dioxane and a mixture of dichloroethane with dimethylformamide	162°	—	4.90, 4.88	4.86	289.1, 287.2	288.3
N-α-Naphthylacetyl-DL-threonine $CH_3CHOHCHNHXCOOH$	87.7	Water	155	—	4.72, 4.76	4.88	288.3, 288.6	287.3
N-α-Naphthylacetyl-DL-phenylalanine $C_6H_5CH_2CHNHXCOOH$	96.2	A mixture of dichloroethane with methyl alcohol and of benzene with isopropyl alcohol	195	—	4.39, 4.44	4.20	332.6, 330.9	333.4
N-α-Naphthylacetyl-DL-aspartic acid $HOOCCH_2CHNHXCOOH$	55.8	A mixture of dichloroethane with methyl alcohol and water	170—171.5	—	4.70, 4.88	4.65	150.4, 150.3	150.6
N-α-Naphthylacetyl-L-asparagine $H_2NOCCH_2CHNHXCOOH$	50	Isopropyl alcohol	193—193.5	+9.89°	9.34, 9.40	9.33	299.2, 298.8	300.3
N-α-Naphthylacetyl-DL-asparagine $H_2NOCCH_2CHNHXCOOH$	34.6	The same	204	—	9.25, 9.32	9.33	305.4, 306.2	300.3
N-α-Naphthylacetyl-L-glutamic acid $HOOCCH_2CH_2CHNHXCOOH$	53.3	Water and a mixture of dichloroethane with dioxane	207	—23.61	4.60, 4.34	4.44	156.1, 155.9	157.6
N-α-Naphthylacetyl-DL-glutamic acid $HOOCCH_2CH_2CHNHXCOOH$	53.3	Water and a mixture of benzene with acetic acid	199	—	4.67, 4.74	4.44	157.3, 159.1	157.6

SUMMARY

In order to study the physiological activity and the mechanism of action of plant growth regulators, we synthesized 15 N-α-naphthylacetylamino acids and of these, 14 compounds have not been described in the literature.

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DIPOLE MOMENTS OF STANNIC CHLORIDE COMPLEXES WITH SOME ALIPHATIC ALCOHOLS. XVII.

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Complex formation between tin tetrachloride and aliphatic alcohols has been studied by a series of investigators. Pfeiffer isolated compounds of the compositions $SnCl_4 \cdot 2CH_3OH$ and $SnCl_4 \cdot 2C_2H_5OH$ [1, 2]. Complex compounds of the type $SnCl_4 \cdot 2ROH$ were studied by Rosenheim and Schnabel [3].

An investigation of the electroconductivity and viscosity of the system $SnCl_4 - C_2H_5OH$ indicated the presence of two complex compounds, $SnCl_4 \cdot 2C_2H_5OH$ and $SnCl_4 \cdot 4C_2H_5OH$ [4]. From an investigation of infrared absorption spectra, Laubengayer and Smith showed that stannic chloride formed a complex compound of the composition $SnCl_4 \cdot 2C_2H_5OH$ with ethyl alcohol [5]. Ford and Marschall confirmed the presence of the complex $SnCl_4 \cdot 2CH_3OH$ by the results of ultraviolet and infrared spectral investigations [6]. Recently, Yu.N. Vol'nov studied the interaction of stannic chloride with aliphatic alcohols by a cryoscopic method and established the presence of molecular compounds of the type $SnCl_4 \cdot 2ROH$ [7].

In this work we present the results of determining the dipole moments of the complex compounds formed by tin tetrachloride with methyl, ethyl, n-butyl, isobutyl and isoamyl alcohols of the composition $SnCl_4 \cdot 2ROH$ and $[SnCl_3 \cdot OR \cdot OHR]_2$.

Results of the Investigation and Discussion

We previously described the method of determining the dipole moments, purifying the tin tetrachloride and benzene and also of preparing benzene solutions of the complexes investigated [8]. Here we will only note that after being dried successively over calcium oxide and metallic sodium and two fractional distillations, the alcohols had the following constants.

Alcohol	B.p.	d^{20}_4	$n^{20}D$
CH_3OH	64.4	0.7917	1.3289
C_2H_5OH	78.4	0.7897	1.3616
n-C_4H_9OH	118.0	0.8093	1.3997
iso-C_4H_9OH	108.2	0.8017	1.3961
iso-$C_5H_{11}OH$	131.4	0.8105	1.4068

We prepared complexes of the type $[SnCl_3 \cdot OR \cdot OHR]_2$ by the method of Laubengayer and Smith [5] by prolonged boiling of $SnCl_4 \cdot 2ROH$ in benzene according to the reaction

$$2[SnCl_4 \cdot 2ROH] = [SnCl_3 \cdot OR \cdot OHR]_2 + 2HCl.$$

The presence of a dimeric complex molecule was demonstrated by the results of cryoscopic investigations.

Tables 1-5 give the results of measuring the specific inductive capacitance (ϵ) and the density (d) and also the calculated values of the molar polarization (P_2) of complexes of the composition $SnCl_4 \cdot 2ROH$ in benzene, relative to the mole fractions of the corresponding complex. Table 6 gives the values of the molar polarization,

TABLE 1

Complex $SnCl_4 \cdot 2CH_3OH$ in C_6H_6
$P_{2\infty} = 850\ cm^3$, $R = 52.33\ cm^3$, $\mu = 6.18$ D

c (in mole fractions)	ε_{20}	d_4^{20}	P_2
0.00075	2.3221	0.8794	826
0.00123	2.3469	0.8805	811
0.00216	2.3963	0.8825	799
0.00271	2.4250	0.8837	791
0.00314	2.4475	0.8847	781
0.00358	2.4704	0.8856	782

TABLE 2

Complex $SnCl_4 \cdot 2C_2H_5OH$ in C_6H_6
$P_{2\infty} = 832\ cm^3$, $R = 61.55\ cm^3$, $\mu = 6.08$ D

c (in mole fractions)	ε_{20}	d_4^{20}	P_2
0.00111	2.3384	0.8802	801
0.00139	2.3522	0.8807	787
0.00272	2.4198	0.8835	777
0.00384	2.4763	0.8859	768
0.00562	2.5668	0.8895	757
0.00735	2.6556	0.8932	748
0.00904	2.7407	0.8947	737

TABLE 3

Complex $SnCl_4 \cdot 2n\text{-}C_4H_9OH$ in C_6H_6
$P_{2\infty} = 848\ cm^3$, $R = 80.18\ cm^3$, $\mu = 6.05$ D

c (in mole fractions)	ε_{20}	d_4^{20}	P_2
0.00354	2.4704	0.8857	826
0.00642	2.6378	0.8922	819
0.00933	2.8065	0.8987	810
0.01190	2.9574	0.9044	799
0.01389	3.0702	0.9089	786

TABLE 4

Complex $SnCl_4 \cdot 2iso\text{-}C_4H_9OH$ in C_6H_6
$P_{2\infty} = 850\ cm^3$, $R = 80.08\ cm^3$, $\mu = 6.06$ D

c (in mole fractions)	ε_{20}	d_4^{20}	P_2
0.00206	2.3925	0.8841	811
0.00325	2.4504	0.8852	802
0.00457	2.5111	0.8868	777
0.00522	2.5440	0.8880	764
0.00543	2.5519	0.8884	766
0.00590	2.5712	0.8893	757
0.00616	2.5885	0.8898	761

TABLE 5

Complex $SnCl_4 \cdot 2iso\text{-}C_5H_{11}OH$ in C_6H_6
$P_{2\infty} = 868\ cm^3$, $R = 89.27\ cm^3$, $\mu = 6.10$ D

c (in mole fractions)	ε_{20}	d_4^{20}	P_2
0.00525	2.5658	0.8883	835
0.00583	2.5886	0.8895	832
0.00653	2.6371	0.8908	827
0.00792	2.7120	0.8935	818
0.00876	2.7567	0.8951	812
0.00970	2.8075	0.8969	808

extrapolated to infinite dilution ($P_{2\infty}$), the refraction (R) and the dipole moments (μ) of all five complexes and the corresponding alcohols (μ'). In the last column is given the difference between the dipole moments of the complex and the polar component in the form $\mu - \mu_1\sqrt{2}$, i.e., it is assumed that the two alcohol molecules are disposed at an angle of 90° to each other in the complex.

The data presented show that the interaction between tin tetrachloride and aliphatic alcohols is accompanied by a considerable increase in the polarity as in the case of complex compounds formed by $SnCl_4$ with other oxygen-containing organic addends [8-10]. The dipole moment of the complex is much greater than the moment of the polar component forming part of the complex, which indicates the appearance of a strongly polarized donor-acceptor covalent bond. The presence of such a bond is confirmed by a series of experimental facts: the high melting points of the complexes (in comparison with the melting points of the components), the considerable electroconductivity of the complex and the low solubility in nonpolar solvents, whose molecules do not have π-bonds.

The presence of a considerable dipole moment in complexes of the type $SnCl_4 \cdot 2ROH$ indicates that the latter have a cis-configuration. Evidently, the cis-form is most stable at normal temperatures for the complexes $SnCl_4 \cdot 2A$ (where A is a molecule of an oxygen-containing organic addend) [8-10]. It is noticeable that the increase in the dipole moment for all the complexes we investigated is constant (Table 6). We proposed that such

TABLE 6

Complex	$P_{2\infty}$	R	μ	μ_1	$\mu-\mu_1\sqrt{2}$
$SnCl_4 \cdot 2CH_3OH$	850	52.33	6.18	1.69	3.80
$SnCl_4 \cdot 2C_2H_5OH$	832	61.55	6.08	1.66	3.74
$SnCl_4 \cdot 2n\text{-}C_4H_9OH$	848	80.18	6.05	1.66	3.73
$SnCl_4 \cdot 2iso\text{-}C_4H_9OH$	850	80.08	6.06	1.67	3.71
$SnCl_4 \cdot 2iso\text{-}C_5H_{11}OH$	868	89.27	6.10	1.76	3.68

TABLE 7

Complex $[SnCl_3 \cdot OC_2H_5 \cdot OHC_2H_5]_2$ in C_6H_6

$P_{2\infty} = 377\ cm^3$, $R = 103.08\ cm^3$, $\mu = 3.53$ D

c (in mole fractions)	ε_{20}	d_4^{20}	P_2
0.00344	2.3354	0.8854	378
0.00467	2.3584	0.8878	380
0.00494	2.3603	0.8882	381
0.00518	2.3638	0.8887	374
0.00577	2.3710	0.8899	372
0.00801	2.4084	0.8943	377

TABLE 8

Complex $[SnCl_3 \cdot OC_4H_9 \cdot OHC_4H_9\text{-}n]_2$ in C_6H_6

$P_{2\infty} = 373\ cm^3$, $R = 140.12\ cm^3$, $\mu = 3.22$ D

c (in mole fractions)	ε_{20}	d_4^{20}	P_2
0.00193	2.3201	0.8884	374
0.00275	2.3360	0.8937	377
0.00411	2.3646	0.9014	371
0.00539	2.3889	0.9088	365
0.00650	2.4167	0.9151	378

TABLE 9

Complex $[SnCl_3 \cdot OC_4H_9 \cdot OHC_4H_9\text{-}iso]_2$ in C_6H_6

$P_{2\infty} = 378\ cm^3$, $R = 140.12\ cm^3$, $\mu = 3.24$ D

c (in mole fractions)	ε_{20}	d_4^{20}	P_2
0.00529	2.3728	0.8971	374
0.00795	2.4112	0.9065	371
0.01044	2.4513	0.9149	379
0.01271	2.4958	0.9227	384

TABLE 10

Complex $[SnCl_3 \cdot OC_5H_{11} \cdot OHC_5H_{11}\text{-}iso]_2$ in C_6H_6

$P_{2\infty} = 382\ cm^3$, $R = 160.53\ cm^3$, $\mu = 3.10$ D

c (in mole fractions)	ε_{20}	d_4^{20}	P_2
0.00266	2.3222	0.8873	382
0.00370	2.3370	0.8911	383
0.00453	2.3481	0.8941	385
0.00559	2.3644	0.8978	377

constancy in the difference $\mu - \mu_1\sqrt{2}$ indicates that the stability of the complex in solution is independent of the length of the alcohol radical. This was previously demonstrated on complexes of stannic chloride with esters of monobasic carboxylic acids [8].

Cryoscopic investigations of the system $SnCl_4$–ROH [7] also indicated that the stability of complexes of the type $SnCl_4 \cdot 2ROH$ depends very little on the nature of the alcohol radical. This independence may probably be explained by the rapid fall in the inductive effect along an alcohol radical. Consequently, the electronic density around the oxygen atom, characterizing its donor properties, is changed very little in replacing one radical by another, which agrees with the general rules for the mutual interaction of atoms established by V.V. Markovnikov.

Laubengayer and Smith [5] established that when boiled in benzene, the complex $SnCl_4 \cdot 2C_2H_5OH$ loses a molecule of HCl and is converted into a compound with the empirical formula $[SnCl_3 \cdot OC_2H_5 \cdot OHC_2H_5]$. A qualitative comparison of the infrared absorption spectra of C_2H_5OH as vapor and liquid and $[SnCl_3 \cdot OC_2H_5 \cdot OHC_2H_5]$

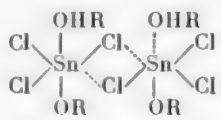
indicated that the latter compound is associated as a dimer with an increase in the coordination number of tin from five to six. We have already noted above that the dimeric character of the complex $[SnCl_4 \cdot OC_2H_5 \cdot OHC_2H_5]$ was confirmed by cryoscopic investigations. Using the method developed by Laubengayer and Smith, we isolated the complexes $[SnCl_4 \cdot OR \cdot OHR]_2$, where R = C_2H_5, n-C_4H_9, iso-C_4H_9 and iso-C_5H_{11}.

The compounds appeared as white, coarsely crystalline substances.

In Tables 7-10 we present the results of measuring the specific inductive capacitance and the density and also the calculated values of the molar polarization of complexes of the type $[SnCl_4 \cdot OR \cdot OHR]_2$ in benzene in relation to the mole fractions of the corresponding complex.

For the complex $[SnCl_4 \cdot OC_2H_5 \cdot OHC_2H_5]_2$, the molar polarization extrapolated to infinite dilution (P_{∞}) equaled 377 cm^3, the deformation polarization ($P_E = P_D + P_A$), 118.50 cm^3 and the dipole moment, 3.54 D. For the three following complexes $[SnCl_4 \cdot OC_4H_9 \cdot OHC_4H_9\text{-n}]_2$, $[SnCl_4 \cdot OC_4H_9 \cdot OHC_4H_9\text{-iso}]_2$ and $[SnCl_4 \cdot OC_5H_{11} \cdot OHC_5H_{11}\text{-iso}]_2$ these values, respectively, equaled 373, 212.05 and 3.22; 378, 212.05 and 3.24; 382, 184.62 cm^3 and 3.10 D.

From the data presented it is obvious that the conversion of the complex $SnCl_4 \cdot 2ROH$ into $[SnCl_4 \cdot OR \cdot OHR]_2$ is accompanied by a sharp fall in polarity. For example, for the complex formed by $SnCl_4$ with ethyl alcohol, this conversion leads to a decrease in molar polarization at infinite dilution of 473 cm^3 and in the dipole moment of 2.64 D. It is clear that the considerable decrease in polarity indicates an increase in the symmetry of the complex molecule. The dipole moments presented for the compounds $[SnCl_4 \cdot OR \cdot OHR]_2$ give grounds for thinking that these compounds have a planar cis-structure in benzene.



The comparatively low values of the dipole moments are evidently characterized by the difference in polarity of the alcohol and its residue, OR. From the data in Tables 7-10 it is evident that the molar polarization P_2 does not change with a change in concentration of the complex. Consequently, with dilution the kinetic particle does not change its molecular state, indicating the considerable stability of the dimer $[SnCl_4 \cdot OR \cdot OHR]_2$. This experimental fact once again indicates the fact that a coordination number of 5 is improbable for tin (in contrast to titanium).

SUMMARY

1. The dipole moments of the complexes $SnCl_4 \cdot 2CH_3OH$, $SnCl_4 \cdot 2C_2H_5OH$, $SnCl_4 \cdot 2n\text{-}C_4H_9OH$, $SnCl_4 \cdot 2\text{-iso-}C_4H_9OH$, and $SnCl_4 \cdot 2\text{-iso-}C_5H_{11}OH$ were determined. On the basis of the values of the moments, a cis-structure may be assigned to the complexes listed.

2. It was shown that the dipole moments of the complexes studied did not depend on the length of the alcohol radical, which agrees with previous investigations.

3. The dipole moments of the complexes $[SnCl_4 \cdot OC_2H_5 \cdot OHC_2H_5]_2$, $[SnCl_4 \cdot OC_4H_9 \cdot OHC_4H_9\text{-n}]_2$, $[SnCl_4 \cdot OC_4H_9 \cdot OHC_4H_9\text{-iso}]_2$ and $[SnCl_4 \cdot OC_5H_{11} \cdot OHC_5H_{11}\text{-iso}]_2$ were determined. It was established that the conversion of $SnCl_4 \cdot 2ROH$ into $[SnCl_4 \cdot OR \cdot OHR]_2$ was accompanied by a sharp decrease in polarity. The most probable structure for the complex $[SnCl_4 \cdot OR \cdot OHR]_2$ is a flat cis-structure.

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INVESTIGATIONS IN THE FIELD OF INDOLE DERIVATIVES

VI. THE MECHANISM OF THE E. FISCHER REACTION. A STUDY OF THE CONVERSIONS OF THE METHYLPHENYLHYDRAZONE OF METHYL ETHYL KETONE

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In a previous communication we showed that when the phenylhydrazone of methyl ethyl ketone was heated with acetic anhydride in the presence of p-toluenesulfonic acid, it gave a high yield of 2-(N,N'-diacetyl-β-phenylhydrazino)-butene-2, which is the diacetyl derivative of an N-hydrazine, the first intermediate product of the E. Fischer reaction, according to the Robinsons' scheme [1]. From the theoretical point of view, a study of

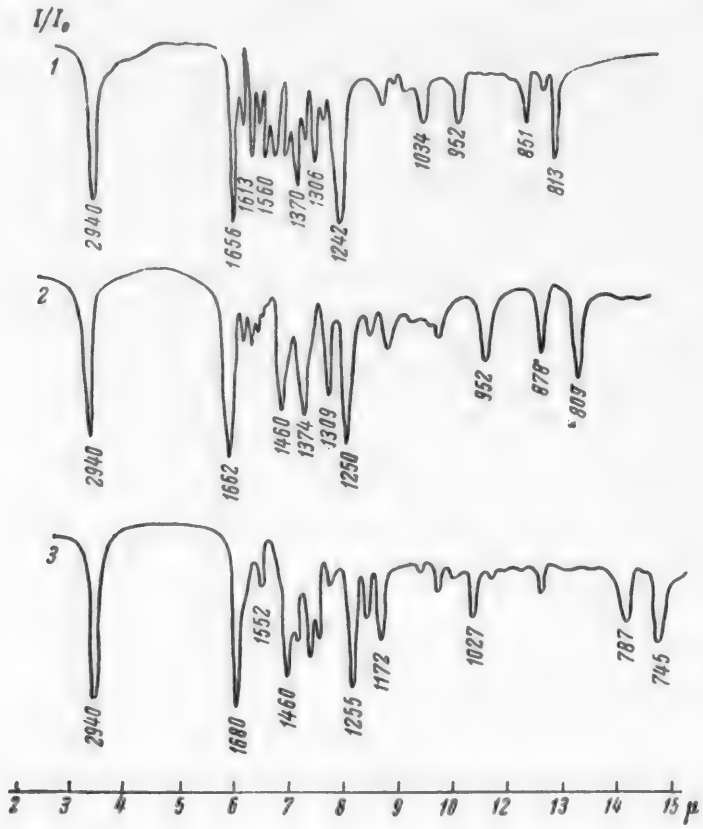


Fig. 1. Infrared absorption spectra: 1) Bz-acetyl-1,2,3-trimethylindole, m.p. 125-126.5°; 2) Bz-acetyl-1,2,3-trimethylindole, m.p. 101.5-102.5°; 3) Bz-acetyl-1,2,3-trimethylindole, m.p. 113.5-114.5°.

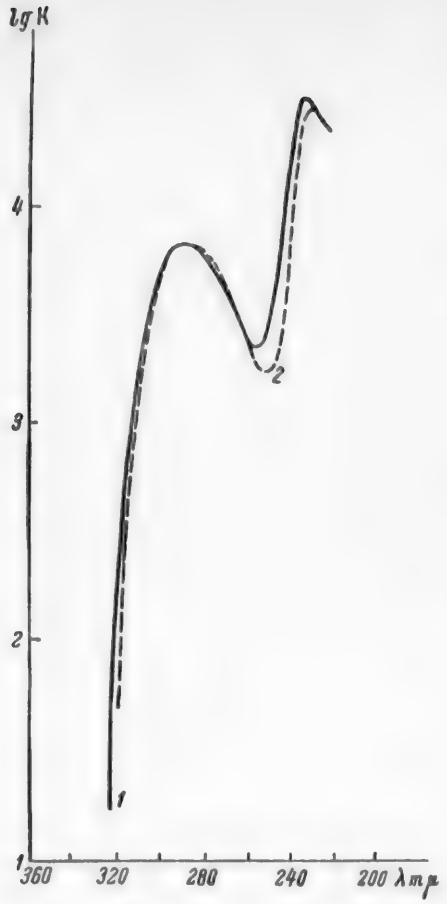


Fig. 2. Ultraviolet absorption spectra: 1) Bz-ethyl-1,3,3-trimethylindole, obtained by reduction of Bz-acetyl-1,2,3-trimethylindole with m.p. 125-126.5°; 2) 1,2,3-trimethylindole.

the behavior of the methylphenylhydrazone of methyl ethyl ketone (I) under analogous conditions was of great interest. One might have supposed that due to the impossibility of stabilizing the unsaturated hydrazo compound as a result of acetylation of the two nitrogen atoms, the reaction must proceed differently in the latter case than with the unsubstituted phenylhydrazone. Experiment confirmed this hypothesis. As a result of vacuum distillation, chromatography on aluminum oxide and repeated recrystallization, the product of boiling the methylphenylhydrazone of methyl ethyl ketone with acetic anhydride in the presence of p-toluenesulfonic acid yielded five substances. One of these was found to be N-methylacetanilide (II) and another β-acetyl-α-methyl-α-phenylhydrazine (III). The formation of these substances is explained by the lower stability of the N–N and C–N bonds due to the absence of stabilization as a result of acetylation of the two nitrogen atoms. The other three compounds were found to be isomeric with each other. They all formed 2,4-dinitrophenylhydrazones, indicating the presence of a carbonyl group. The elementary composition and the capacity to form red picrates indicated that these substances were isomeric acetyl-1,2,3-trimethylindoles, differing in the position of the acetyl group in the benzene ring.

This hypothesis was confirmed by data from the infrared spectra. The spectra of all three compounds contained a series of closely placed bands, bands of NH (and OH) groups were absent and intense carbonyl absorption bands were observed in the region 1650-1680 cm^{-1} (Fig. 1).

The position of the carbonyl bands was characteristic of certain classes of compounds, in particular, it is observed in the spectra of aromatic ketones (acetophenone, aminoacetophenone, etc. [2]); in addition, it is connected with the presence of a ketone group, conjugated with an aromatic nucleus, containing electron-donor substituents. It is obvious that acetyl-1,2,3-trimethylindole may be considered as a compound of just this type, whereby in this case, the electron-donor group is the nitrogen atom of the five-membered ring.

Considering that the strongest shift of the carbonyl band toward lower frequencies may be expected for para-substituted derivatives of such a nature and the least for meta-substituted derivatives, on the basis of spectral data, one may tentatively establish the position of the acetyl residue in each of the acetyl-1,2,3-trimethylindole isomers isolated.

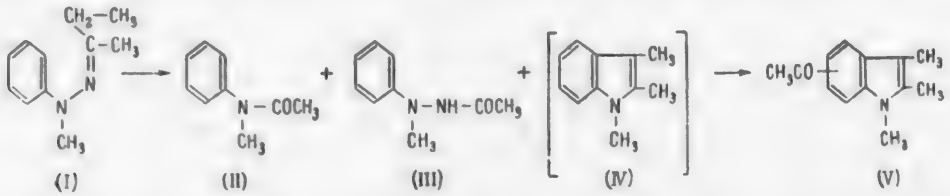
The hypothetical identification of the compounds, which we made on this basis, is presented in the experimental; we should note that it is not final and requires confirmation by chemical methods.

In connection with this and also to obtain additional proof of the indole nature of the compounds obtained, these compounds were reduced by the Huang-Minlon modification of the Kizhner method. This yielded three corresponding isomeric substances, whose infrared spectra lacked the carbonyl-group band and whose ultraviolet spectra were in close agreement with the spectrum of 1,2,3-trimethylindole (Fig. 2).

On the basis of these data and elementary analysis data, one may conclude that the substances obtained by reduction were isomeric Bz-ethyl-1,2,3-trimethylindoles. The position of the ethyl group in each of these is being elucidated by synthesis at the present time.

It seemed to us that the formation of Bz-acetyl-1,2,3-trimethylindoles should be explained by subsequent

acetylation of 1,2,3-trimethylindole (IV), the normal product of the Fischer reaction. To prove this hypothesis, 1,2,3-trimethylindole was boiled with acetic anhydride in the presence of p-toluenesulfonic acid under the same conditions as with the methylphenylhydrazone of methyl ethyl ketone. Actually, from the reaction mixture, we isolated the same Bz-acetyl-1,2,3-trimethylindoles as in the case of the latter. Thus, one may consider the following scheme for the conversions of the methylphenylhydrazone of methyl ethyl ketone as proved.



(I) (II) (III) (IV) (V)

It is easy to see the reason for the different behavior of the phenylhydrazone and the methylphenylhydrazone of methyl ethyl ketone in the reaction examined. In the first case, the reaction stops at the stage of the acetyl derivative of the unsaturated hydrazine, whose stability is explained by the fact that the free electron pairs at the two nitrogen atoms are fixed by acetylation. In the case of the methylphenylhydrazone, the electron pair at the nitrogen, directly attached to the benzene ring, remain free and due to this a molecular rearrangement is possible which finally leads to 1,2,3-trimethylindole (IV). In the interesting work of A.E. Arbuzov and Yu.P. Kitaev on the mechanism of the Fischer reaction [3], particular stress was laid on the role of the nitrogen atom removed from the aromatic ring, to which the addition of a proton or the formation of a complex would strongly polarize the N—N and C=C bonds.

The acetylation of this atom must also act similarly, which also confirms our observations. In the case where the nitrogen atom directly connected to the benzene ring is acetylated, then the ease with which the Fischer reaction proceeds must be strongly reduced due to the fall in polarity of the N—N bond, as was observed by Perkin and Plant [4] in the conversion of the α-acetyl-α-phenylhydrazone of cyclohexanone into 9-acetyl-1,2,3,4-tetrahydrocarbazole. Unfortunately, this acetylphenylhydrazone, obtained by heating the phenylhydrazone with acetic anhydride, was not characterized sufficiently fully. Finally, with acetylation of both nitrogen atoms in the N-hydrazine, the polarity of the N—N bond falls so much that the Fischer reaction cannot proceed further.

At the same time, we cannot agree with the opinion of A.E. Arbuzov and Yu. Kitaev that the Robinson scheme has an unnecessary stage, the formation of the unsaturated diamine, since we obtained such a diamine previously in the form of the acetyl derivative [1]. The problem of the exact character of the molecular rearrangement in the Fischer reaction requires further experimental study.

EXPERIMENTAL

The methylphenylhydrazone of methyl ethyl ketone (I) was prepared by boiling 1 mole of asymmetric methylphenylhydrazine with 2.5 moles of methyl ethyl ketone for one hour with subsequent vacuum distillation. The b.p. was 80-83° (2 mm).

Interaction of the methylphenylhydrazone of methyl ethyl ketone with acetic anhydride. 33 g of the methylphenylhydrazone of methyl ethyl ketone was boiled for one hour with 193 g of acetic anhydride and 0.772 g of p-toluenesulfonic acid monohydrate. To the still hot solution was added 0.38 g of crystalline sodium acetate, the acetic anhydride removed in vacuum and the residue treated with 100 ml of water. The substance was extracted four times with 150-ml portions of ether. After drying over magnesium sulfate, the ether was evaporated and the residue vacuum distilled to give the following fractions: 1st, 4.5 g, b.p. 86-120° (2 mm); 2nd, 8 g, b.p. 120-175° (1.5 mm); 3rd, 11.6 g, b.p. 175-177° (1.5 mm).

The first fraction was a colorless, crystalline substance. The m.p. was 99-100.5° (from aqueous alcohol). According to elementary analysis and infrared spectral [5] data, this substance was methylacetanilide, which was confirmed by direct comparison with an authentic sample.

Found %: C 72.56, 72.67; H 7.59, 7.90; N 9.77, 9.37. $C_9H_{11}ON$. Calculated %: C 72.48; H 7.39; N 9.39.

The second fraction was a mixture of substances, which was resolved chromatographically. For this purpose,

a solution of 8 g of the substance in 500 ml of n-heptane was passed through a column containing 160 g of aluminum oxide. A mixture of n-heptane and benzene (4:1) yielded fraction "A," which was a mixture of substances that could not be separated by recrystallization. With mixtures of n-heptane and benzene (3:2, 1:1, 2:3, 1:4) and benzene, we obtained a substance, which had m.p. 125-126.5° after recrystallization from n-hexane (weight 0.3 g) and was identical with the product forming the bulk of fraction 3. Mixtures of benzene and ether (4:1, 1:1)and ether eluted a substance with m.p. 91.5-92.5° (from n-hexane). According to elementary analysis data and the infrared spectrum [the presence of bands corresponding to the N−H group (3260 cm^{-1}), an amide carbonyl group (1662 cm^{-1}) and a phenyl ring (1597 and 1542 cm^{-1})], this substance was acetylmethylphenylhydrazine, as was confirmed by direct comparison with a sample synthesized.

Found %: C 66.06, 66.15; H 7.52, 7.52; N 16.85. $C_9H_{12}ON_2$. Calculated %: C 65.85; H 7.31; N 17.06.

1 g of mixture (A) obtained was dissolved in 150 ml of n-heptane and chromatographed a second time on 20 g of aluminum oxide. With a mixture of n-heptane and benzene (19:1), the first three fractions (30 ml each) yielded 0.35 g of a substance, which had m.p. 113.5-114.5° after two recrystallizations from n-hexane. According to elementary analysis data and the infrared spectrum, this substance was an isomer of the substance from the third fraction. It had the composition of acetyltrimethylindole, gave a red precipitate with 2,4-dinitrophenylhydrazine and formed a picrate with m.p. 145-146.5°. Since a C=O band was observed in the infrared spectrum of the substance at 1680 cm^{-1}, one may postulate that it was 6- or 4-acetyl-1,2,3-trimethylindole.

Found %: C 77.35, 77.02; H 7.36, 7.07; N 6.84. $C_{13}H_{15}ON$. Calculated %: C 77.61; H 7.46; N 6.96.

Further elution with the same mixture yielded 0.45 g of a substance with m.p. 101.5-102.5° (many recrystallizations from n-hexane), which, according to elementary analysis data and the infrared spectrum, was an isomer of the previously described acetyltrimethylindoles. From the position of the C=O band (1662 cm^{-1}), it is most probable that this was 7-acetyl-1,2,3-trimethylindole. This isomer gave a red precipitate with 2,4-dinitrophenylhydrazine and formed a picrate with m.p. 156-157.5°.

Found %: C 77.11; H 7.39; N 6.68, 6.73. $C_{13}H_{15}ON$. Calculated %: C 77.61; H 7.46; N 6.96.

The third fraction was a pale-yellow, crystalline substance. The m.p. was 126-126.5° (after several recrystallizations from aqueous alcohol and carbon tetrachloride). According to elementary analysis data and UV and IR spectra, this substance was acetyltrimethylindole. From the position of the C=O band (1656 cm^{-1}) in the infrared spectrum, one may postulate that the substance was 5-acetyl-1,2,3-trimethylindole.

Found %: C 77.75, 77.99; H 7.37, 7.42; N 6.92, 7.28. $C_{13}H_{15}ON$. Calculated %: C 77.61; H 7.46; N 6.96.

The substance formed a picrate as dark-red needles with m.p. 120.5-121.5°.

Found %: C 53.73, 53.58; H 3.88, 4.23; N 12.56, 13.11. $C_{13}H_{15}ON \cdot C_6H_2(NO_2)_3OH$. Calculated %: C 53.02; H 4.05; N 13.02.

The 2,4-dinitrophenylhydrazone was a reddish, crystalline substance with m.p. 277-278°.

Found %: N 17.90, 17.80. $C_{19}H_{19}O_4N_5$. Calculated %: N 18.37.

1,2,3-Trimethylindole (IV). 40 g of the methylphenylhydrazone of methyl ethyl ketone was boiled with 78 g of concentrated sulfuric acid in 150 ml of anhydrous alcohol. When cool, the substance was poured into 1.5 liters of water and the substance extracted with ether. After drying over sodium sulfate, the ether was evaporated and the residue vacuum-distilled to give a fraction with b.p. 103-105° (1 mm). The yield of 1,2,3-trimethylindole was 22 g (62.5%).

Found %: C 83.34; H 8.07; N 9.28. $C_{11}H_{13}N$. Calculated %: C 83.01; H 8.17; N 8.81.

Literature data [6]: m.p. 18°, b.p. 283-284° (750 mm).

Acetylation of 1,2,3-trimethylindole. 22 g of 1,2,3-trimethylindole was boiled for one hour with 143.6 g of acetic anhydride and 0.575 g of p-toluenesulfonic acid monohydrate. Treatment of the reaction mixture as described earlier yielded three fractions: 1st, 3.5 g, b.p. 150-174° (2.5 mm); 2nd, 9.3 g, b.p. 174-175° (2 mm), 3rd, 3.5 g, b.p. 175-177° (2 mm).

Chromatography of the first fraction on aluminum oxide gave 1.45 g of acetyltrimethylindole with m.p. 113.5-114.5° (picrate melted at 145-146°) and 1.6 g of an isomer with m.p. 125-126°, identical with the compounds described previously. Chromatography of the second fraction on aluminum oxide yielded 0.6 g of a substance with m.p. 113.5-114° and 1.4 g of an isomeric acetyltrimethylindole with m.p. 101-102° (picrate melted at 156-157°) and 6.5 g of an isomer with m.p. 125.5-126.5°. These compounds were also identical with the corresponding acetyltrimethylindoles obtained from the methylphenylhydrazone of methyl ethyl ketone. Finally, after recrystallization from n-hexane, the third fraction gave only the isomer with m.p. 125-126.5°, which was also identical with the high-melting isomer from the experiment described previously.

Reduction of the isomeric acetyl-1,2,3-trimethylindoles by the Kizhner reaction. A mixture of 1.5 g of acetyl-1,2,3-trimethylindole with m.p. 126-126.5°, 1.05 g of sodium hydroxide, 1.05 g of hydrazine hydrate (99.9%) and 35 ml of diethylene glycol was boiled for one hour. Then heating was continued with the simultaneous distillation of water until the temperature of the reaction mixture reached 190-200°. The mixture was boiled at this temperature for three hours. When the mixture had cooled, 120 ml of water was added and the reduction product steam-distilled. The distillate was extracted with ether. The extract was dried over sodium sulfate, the ether removed and vacuum distillation of the residue yielded 1.2 g of a substance with b.p. 139-141° (7 mm). The analysis data corresponded to ethyl-1,2,3-trimethylindole.

Found %: C 87.79, 83.64; H 9.43, 9.20; N 7.68. $C_{13}H_{17}N$. Calculated %: C 83.42; H 9.09; N 7.43.

The picrate formed red needles with m.p. 120-121°.

Found %: C 55.05, 55.03; H 4.92, 4.66; N 12.78, 12.70. $C_{13}H_{17}N \cdot C_6H_2(NO_2)_3OH$. Calculated %: C 54.80; H 4.80; N 13.47.

Similarly, from acetyl-1,2,3-trimethylindole with m.p. 113.5-114.5° we obtained ethyl-1,2,3-trimethylindole as a crystalline substance with m.p. 40.5-41° (the picrate had m.p. 44-46°).

Elementary analysis and the IR spectrum indicated that this substance was an isomeric ethyl-1,2,3-trimethylindole.

Found %: C 83.23; H 8.68; N 7.27, 7.28. $C_{13}H_{17}N$. Calculated %: C 83.42; H 9.09; N 7.48.

The low-melting acetyl-1,2,3-trimethylindole (m.p. 101.5-102.5°) yielded ethyl-1,2,3-trimethylindole with b.p. 115-120° (3 mm) as a pale-yellow, nonlabile oil which rapidly darkened on standing. Due to its instability, the substance was analyzed as the picrate with m.p. 118-120°.

Found %: C 54.22; H 5.36; N 12.81. $C_{13}H_{17}N \cdot C_6H_2(NO_2)_3OH$. Calculated %: C 54.8; H 4.8; N 13.47.

All the infrared spectra were obtained with an IKS-11 spectrometer (NaCl prism). The substances were examined as suspensions in vaseline oil (for crystalline compounds) or as thin layers (for liquids).

The ultraviolet spectra were plotted on an SF-4 spectrophotometer. Ethyl alcohol was used as the solvent.

SUMMARY

1. A study was made of the reaction of the methylphenylhydrazone of methyl ethyl ketone when heated with acetic anhydride in the presence of p-toluenesulfonic acid. It was established that the behavior of this substance in this reaction differed from the behavior of the phenylhydrazone of methyl ethyl ketone.

2. It was shown that the products of the above reaction were methylacetanilide, acetylmethylphenylhydrazine and also three isomers of acetyl-1,2,3-trimethylindole.

3. It was established that the latter were the products of further acetylation of 1,2,3-trimethylindole, formed from the methylphenylhydrazone of methyl ethyl ketone by a normal Fischer reaction.

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SYNTHESIS AND POLYCONDENSATION OF p-AMINOMETHYLPHENYLALKANECARBOXYLIC ACIDS

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Polyamides containing benzene nuclei in the macromolecular chains in addition to methylene and amide groups are of interest for the preparation of high-melting synthetic fibers. The most convenient polyamides for this purpose are those of the homopolycondensation type from unbranched α,ω-amino acids, containing p-phenylene groups in the methylene chains. As practice has shown, heteropolycondensation polyamides are less heat-stable, which complicates the technology of their production and spinning.

Depending on the mutual disposition of the benzene nuclei and the functional groups, α,ω-amino acids may be divided into p-(ω-aminoalkyl)-benzoic, p-$NH_2(CH_2)_nC_6H_4COOH$, p-aminophenylalkanecarboxylic, p-$NH_2C_6H_4(CH_2)_nCOOH$ and p-(ω-aminoalkyl)-phenylalkanecarboxylic acids, p-$NH_2(CH_2)_nC_6H_4(CH_2)_n$-COOH. When heated, p-($\omega$-aminoalkyl)-benzoic acids decompose [1] and p-aminophenylalkanecarboxylic acids form polyamides, which decompose in the fused state [2]. p-(ω-Aminoalkyl)-phenylalkanecarboxylic acids have not been described in the literature. However, they deserve the most attention since their structure is most similar to that of α,ω-amino acids, which form heat-stable, fiber-forming polyamides.

In the present work we synthesized p-aminomethylphenylacetic (I), p-aminomethylphenylpropionic (II), p-aminomethylphenylbutyric (III) and p-aminomethylphenylvaleric acids (IV), $NH_2CH_2C_6H_4(CH_2)_nCOOH$ (n = 1-4). The starting compounds were the corresponding p-chloromethylphenylalkanecarboxylic acids, which we prepared previously by chloromethylation of phenylalkanecarboxylic acids [3]. Since the chloromethyl group of these compounds could not be aminated directly with ammonia, the amino acids were synthesized by decomposition of the complexes of urotropin with the p-halomethylphenylalkanecarboxylic acids.

As recommended [4], for preparing the urotropin complexes, p-chloromethylphenylacetic, p-chloromethylphenylpropionic and p-chloromethylphenylvaleric acids were converted into the corresponding p-iodomethylphenylalkanecarboxylic acids. However, this operation was found to be unnecessary. Thus, the yield of the urotropin complex obtained directly from p-chloromethylphenylbutyric acid was almost quantitative; it is true that the reaction proceeded more slowly, but the decomposition products of the complex were not contaminated with elementary iodine.

The amino acid hydrochlorides obtained by decomposition of the urotropin complexes were converted into the free amino acids by evaporation of an ammonia solution of them to dryness. The residue was a mixture of ammonium chloride and the free amino acid, which was freed from mineral impurities by recrystallization from water.

The amino acids synthesized did not have definite melting points; in contrast to most amino acids, they were moderately soluble in water; when heated they were converted into high-molecular polyamides.

It was found that the polyamides were not only formed by maintaining the substance in a molten state. High-molecular polyamides were also formed from the amino acids synthesized at temperatures below the melting point of the polymer (in the solid phase), which is particularly important for the preparation of thermally unstable polymers. The polyamides from (III) and (IV) were tough, white, horny bodies, whose melts formed tough fibers which could be drawn in the cold. The polyamides from (I) and (II) decomposed when fused and, therefore,

Polyamides from p-Aminomethylphenylalkanecarboxylic Acids

Starting amino acids	Polycondensation conditions		Properties of polyamides				
	temperature	duration (min)	character of product	specific viscosity*	melting point	solubility in phenol, tricresol, and formic acid	fiber-forming properties
p-$NH_2CH_2C_6H_4(CH_2)_4COOH$	265°	60	White, horny, tough	0.77	227—233°	Soluble	Forms tough fibers
p-$NH_2CH_2C_6H_4(CH_2)_3COOH$	260	60	Fused, white lumps	0.55	265—267	The same	The same
	290	30	White, horny, tough	0.49			
p-$NH_2CH_2C_6H_4(CH_2)_2COOH$	280	30	Fused, white lumps	0.47	295—300	" "	Forms weak fibers
	325	15	Yellow, horny	0.35			
p-$NH_2CH_2C_6H_4CH_2COOH$	295	40	White powder	—	350—355 (with decomposition)	Insoluble	Does not form fibers

*The specific viscosity was determined for a 0.5% solution of polyamide in tricresol.

tough fibers could not be formed from the melts. When the length of the chain of the polyamide was reduced by one methylene group in the order (IV), (III), (II), the melting point rose by approximately 30° and in going from (II) to (I), by 60°. The sharp rise in melting point of the polyamide from (I), is apparently connected not only with the increase in the relative content of amide groups, but also with the increase in the packing density of the macromolecules due to the symmetry of the elementary units of the polyamide.

EXPERIMENTAL

Synthesis of amino acids. p-Aminomethylphenylvaleric acid (IV). 25.0 g of p-chloromethylphenylvaleric acid and 17.5 g of NaI were dissolved in 125 ml of acetone. The solution was boiled for 30 minutes, the liberated NaCl filtered off and the filtrate evaporated to dryness. The residue was dissolved in 300 ml of hot benzene, the solution decolorized by shaking with thiosulfate solution and the solvent evaporated.

The residue was dissolved in 150 ml of boiling chloroform, a solution of 17.5 g of urotropin in 150 ml of chloroform gradually added through the reflux condenser and the solution boiled for 40 minutes. We obtained 43.0 g of urotropin complex (85%). The complex was dissolved in 50 ml of concentrated hydrochloric acid by gentle heating and the solution mixed with 140 ml of ethanol and boiled for one hour. The mineral salt was filtered off and washed with ethanol. The filtrate was concentrated by evaporation of the formal and alcohol to a volume of 50 ml, mixed with 100 ml of dilute (1:1) hydrochloric acid, evaporated to the consistency of a thick syrup* and crystallized from 100 ml of concentrated hydrochloric acid. The hydrochloride of the amino acid was dissolved in 200 ml of water, the solution neutralized with ammonia until a precipitate began to form and extracted four times with ether to remove traces of elementary iodine. The extracted solution was mixed with 60 ml of 20% ammonia. The substance liberated was crystallized from 350 ml of 4% ammonia. A small amount of amino acid was obtained in addition by evaporation of the mother solutions. Recrystallization from 380 ml of 4% ammonia (by solution and boiling the

*Necessary to hydrolyze the ethyl ester of the amino acid.

solution until crystals appeared) yielded 12.5 g of p-aminomethylphenylvaleric acid (needles). The yield was 64%.

Found %: C 69.72, 69.80; H 8.24, 8.25; N 6.75, 6.75. $C_{12}H_{17}O_2N$. Calculated %: C 69.53; H 8.26; N 6.76.

p-Aminomethylphenylpropionic acid (II). The p-iodomethylphenylpropionic acid and the urotropin complex were obtained in the same way as in the previous experiment. 54 g of the urotropin complex was decomposed with 54 ml of concentrated hydrochloric acid and 100 ml of ethanol. After removal of the mineral precipitate, the solution was concentrated to a volume of 50 ml, diluted with concentrated hydrochloric acid (50 ml) and evaporated to dryness. The residue was dissolved in 100 ml of water, filtered, made alkaline with ammonia and evaporated to dryness. The residue was recrystallized from 250 ml of water and the mother solution evaporated to a volume of 70 ml. The amino acid was recrystallized from 320 ml of water and the mother solution evaporated to a volume of 100 ml. We obtained 10.8 g of p-aminomethylphenylpropionic acid as coarse, prismatic crystals. The yield was 48%.

Found %: C 66.97, 66.81; H 7.44, 7.46; N 7.97, 7.87. $C_{10}H_{13}O_2N$. Calculated %: C 67.01; H 7.37; N 7.82.

p-Aminomethylphenylacetic acid (I). The synthesis was accomplished mainly by the procedure used for preparing the previous amino acid. Due to the low solubility of p-iodomethylphenylacetic acid in chloroform, dichloroethane was used for the preparation of the urotropin complex. The yield of the amino acid was 21%, calculated on the urotropin complex.

Found %: C 65.23, 65.36; H 6.59, 6.57; N 8.61, 8.75. $C_9H_{11}O_2N$. Calculated %: C 65.43; H 6.71; N 8.48.

p-Aminomethylphenylbutyric acid (III). The urotropin complex was obtained directly from p-chloromethylphenylbutyric acid and urotropin. The complex was decomposed and the intermediate products treated as in the previous experiments. The yield of p-aminomethylphenylbutyric acid (leaflets from water) was 30%, calculated on the urotropin complex.

Found %: C 67.75, 67.93; H 7.96, 7.93; N 7.31, 7.23. $C_{11}H_{15}O_2N$. Calculated %: C 68.37; H 7.82; N 7.25.

Polycondensation of amino acids. The polycondensation of the amino acids was carried out in tubes in glass sleeves heated with Wood's alloy and through which pure nitrogen was circulated. The results of some polycondensation experiments are presented in the table.

SUMMARY

1. p-Aminomethylphenylacetic, p-aminomethylphenylpropionic, p-aminomethylphenylbutyric and p-aminomethylphenylvaleric acids, which are not described in the literature, were synthesized.

2. Polyamides containing benzene nuclei were obtained from the amino acids named and some of their properties were studied.

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SYNTHESIS OF THIACARBOCYANINES FROM 5-SUBSTITUTED 2-METHYL-6,7-TETRAMETHYLBENZTHIAZOLE

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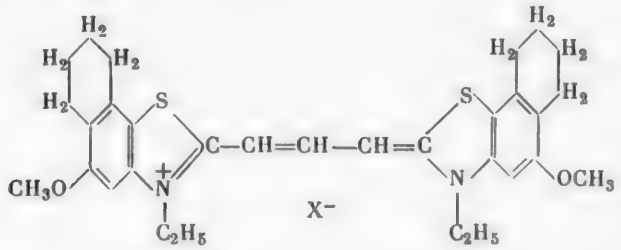
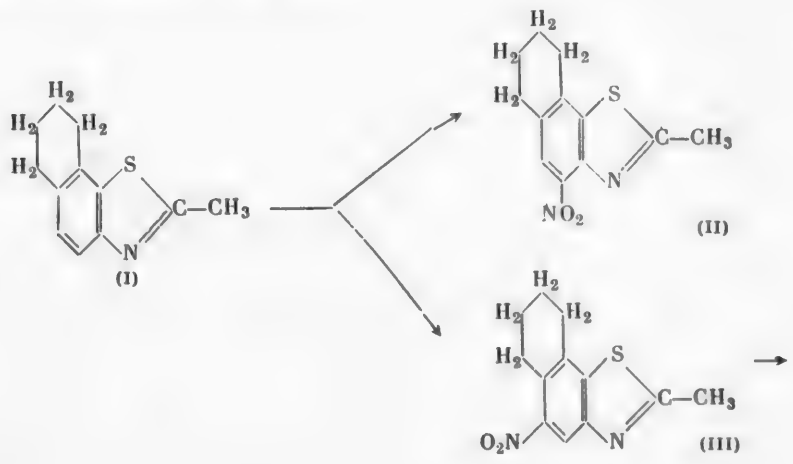
Thiacarbocyanines, containing methoxy groups in the benzthiazole nuclei, have been described previously [1, 2]. With this series of dyes, it was established that the introduction of methoxy groups into the 5,5'- or 6,6'-positions of the thiacarbocyanine molecule considerably shifted the absorption maximum into the long-wave region of the spectrum.

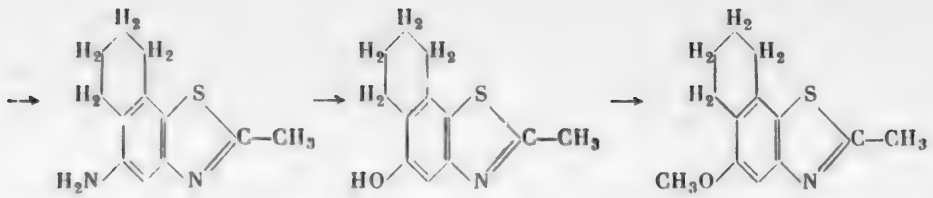
In the present work we present the synthesis of 3,3'-diethyl-6,7,6',7'-bis-(tetramethylene)-thiacarbocyanines, containing methoxy groups in the 5,5'-positions.



In addition, 6,7,6',7'-bis-(tetramethylene)-thiacarbocyanines were prepared with nitro, acetamino and hydroxy groups in the hetero residues.

The starting base was synthesized by the scheme

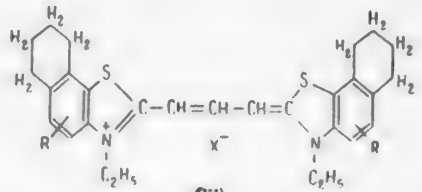




On nitration of base (I), one might expect the formation of a mixture of two isomers, (II) and (III). The nitro product isolated from the reaction mixture had m.p. 92-103°. By fractional crystallization from alcohol, it was possible to isolate two substances from it, one with m.p. 139-140° (yield 32%) and the other with m.p. 96-97° (yield 18.6%). The yield of the nitro derivatives was, to a large extent, dependent on the nitration temperature. In our experiments, this temperature did not exceed −5°. Nitration at higher temperatures led to tar formation.

E.D. Sych [3] showed that the introduction of acetamino groups into the 5,5'- or 6,6'-positions of thiacarbocyanine led to a stronger deepening in color than the introduction of the same groups into the 4,4'- or 7,7'-positions. It was also found [3] that 5,5'-dinitro substituted thiacarbocyanines had an absorption maximum shifted by 22-25 mμ into the short-wave region of the spectrum in comparison with 4,4'-, 6,6'- or 7,7'-dinitrothiacarbocyanines, whose absorption maxima were almost identical and lay within the limits of 582-585 mμ.

We prepared thiacarbocyanines from nitro compounds (II) and (III); reduction of (II) and (III) yielded amines and their acetyl derivatives, which were then converted into quaternary salts and dyes.



(IV)

On comparing the absorption maxima of the dyes we synthesized (Table 1) with the data obtained by Sych [3], one arrives at the conclusion that the isomer with m.p. 96-97° was 2-methyl-4-nitro-6,7-tetramethylenebenzthiazole (II) and the isomer with m.p. 139-140° was 2-methyl-5-nitro-6,7-tetramethylenebenzthiazole (III).

TABLE 1

Absorption Maxima of Thiacarbocyanines (IV)

M.p. of the starting nitrobenzthiazoles	Absorption maxima of the thiacarbocyanines (in mμ)	
	R = NO_2	R = $NHCOCH_3$
96-97°	573	577
139-140	567	586

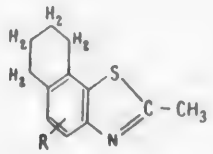
We ran into great difficulties in replacing the amino group by a hydroxyl group in 2-methyl-5-amino-6,7-tetramethylenebenzthiazole. When the diazo solution was poured into boiling water, a substance precipitated, which dissolved in acids, but which was completely insoluble in organic solvents. We were unable to isolate the corresponding hydroxy derivative from it. No substitution of an amino group by a hydroxy group in the benzthiazole series is described. We therefore considered it advantageous to develop this reaction on the example of 2-methyl-5-aminobenzthiazole.

The 2-methyl-5-aminobenzthiazole required was obtained by reduction of 2-methyl-5-nitrobenzthiazole, which is described in the literature [4]. We made certain modifications in the method of synthesizing 2-methyl-5-nitrobenzthiazole. By direct replacement of the bromine atom by the SNa group in 2-bromo-5-nitroaniline, with subsequent acetylation and closure of the thiazole ring, we obtained 2-methyl-5-nitrobenzthiazole in 56% yield.

We were unable to obtain 2-methyl-5-hydroxybenzthiazole by diazotization of 2-methyl-5-aminobenzthiazole in a threefold excess of sulfuric acid and adding the diazo solution obtained to boiling water. It was found that if diazotized 2-methyl-5-aminobenzthiazole was introduced into the theoretically required amount of sulfuric acid, then it was possible to obtain 2-methyl-5-hydroxybenzthiazole in 40% yield. Under the same condition, 2-methyl-6-hydroxybenzthiazole was obtained in 30% yield and 2-methyl-5-hydroxy-6,7-tetramethylenebenzthiazole in 54% yield. Treatment of 2-methyl-5-hydroxy-6,7-tetramethylenebenzthiazole in an alkaline solution with dimethyl sulfate, gave a 76% yield of the corresponding methoxy derivative. The new bases we synthesized are presented in Table 2.

TABLE 2

Substituted 2-Methyl-6,7-tetramethylenebenzthiazoles

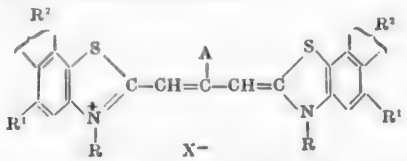


Substituents	Yield (in %)	Melting point
4-NO_2	18	96- 97°
5-NO_2	32	139-140
4-NH_2	53	129-130
5-NH_2	76	156-158
4-$NHCOCH_3$	63	164-165
5-$NHCOCH_3$	77	230-232
5-OH	54	255-256
5-OCH_3	66	88- 89

When treated with diethyl sulfate, the new bases obtained were converted into ethyl ethylsulfates, which were then condensed with orthoesters of carboxylic acids. By reacting β-bromopropionic acid with 2-methyl-5-methoxy-6,7-tetramethylenebenzthiazole, we obtained the corresponding quaternary salt, which was also converted into a dye. The absorption maxima of the thiacarbocyanines synthesized were determined in ethyl alcohol (Table 3).

TABLE 3

Absorption Maxima of Thiacarbocyanines



R	R¹	R²	Absorption maxima (in mμ), A		
			H	CH_3	C_2H_5
C_2H_5	H	H	557	543	547
C_2H_5	H	$-(CH_2)_4-$	572*	556*	562*
C_2H_5	OH	H	575	—	—
C_2H_5	OCH_3	H	576	556	562
C_2H_5	OH	$-(CH_2)_4-$	596	579	570
C_2H_5	OCH_3	$-(CH_2)_4-$	596	580	575
$(CH_2)_2COOH$	OCH_3	$-(CH_2)_4-$	—	—	580

*The dyes were prepared by I.I. Levkoev and N.N. Sveshnikov.

The data in Table 3 show that the introduction of a hydroxy or a methoxy group into the 5,5'-positions of 6,7,6',7'-bis-(tetramethylene)-thiacarbocyanine produced a shift in the absorption maximum into the long-wave region of the spectrum by 24 mμ, while the introduction of the same groups into the 5,5'-positions of the unsubstituted carbocyanine produced a shift of only 18-19 mμ.

In the series of mesoalkyl substituted dyes, the introduction of hydroxy and methoxy groups into the 5,5'-positions of carbocyanines containing tetramethylene groups in the 6,7,6',7'-positions also produced deepening of the color, which was 23-24 mμ for mesomethyl substituted and only 8-13 mμ for mesoethyl substituted compounds. When the ethyl groups on the nitrogen atom were replaced by β-carboxyethyl groups, there was an insignificant deepening in color.

EXPERIMENTAL

2-Methyl-5- and 2-methyl-4-nitro-6,7-tetramethylenebenzthiazoles. Into a flask of 200-ml capacity was placed 50 ml of sulfuric acid (d 1.84), which was cooled to 0°, and to it was gradually added 30.4 g (0.15 mole) of 2-methyl-6,7-tetramethylenebenzthiazole, so that the temperature did not exceed 20°. The flask was fitted with a stirrer, a dropping funnel and a thermometer, the solution cooled to −5° and a mixture of 20 g of nitric acid (d 1.51) and 35 g of sulfuric acid (d 1.84) was added dropwise to it over a period of one hour with vigorous stirring at −5° (not above). After the addition of the nitrating mixture, the mass was stirred at −5° for one hour and then poured onto 1 kg of ice and left overnight. The precipitated mass was ground up, washed with water and dried in air. The weight was 35 g and the m.p. 92-103°. The precipitate was dissolved in 180 ml of alcohol by boiling and the solution filtered and cooled to room temperature. The crystals which precipitated after one hour were filtered off and washed with 20 ml of alcohol. The weight was 18.8 g and the m.p. 124-130°. Two recrystallizations from alcohol yielded light-yellow needles of 2-methyl-5-nitro-6,7-tetramethylenebenzthiazole with m.p. 139-140°. The yield was 11.8 g (32%).

Found %: N 11.00, 10.90. $C_{12}H_{12}O_2N_2S$. Calculated %: N 11.28.

The mother solutions were combined and evaporated to a volume of 50 ml. Cooling liberated a dark tar. The light-yellow solution was decanted and left for four days. The precipitated needles of 2-methyl-4-nitro-6,7-tetramethylenebenzthiazole was filtered off, washed with alcohol and dried. The yield was 6.8 g (18.6%) and the m.p. 96-97°. The melting point was not changed by recrystallization from alcohol.

Found %: N 11.10, 10.94. $C_{12}H_{12}O_2N_2S$. Calculated %: N 11.28.

It was not possible to isolate a base from the dark tar.

2-Methyl-5-amino-6,7-tetramethylenebenzthiazole. Into a flask was placed 12 g of 2-methyl-5-nitro-6,7-tetramethylenebenzthiazole and 60 ml of hydrochloric acid (d 1.19). After solution of the nitro compound, 6 g of tin sponge was added at 55° over a period of 1.5 hours. The mixture was stirred for a further three hours at 55° and left overnight. The precipitated double salt of tin was dissolved in 70 ml of water. The solution was filtered and neutralized with 40% sodium hydroxide with cooling. The precipitated oil crystallized. The precipitate was filtered off, washed with water, dried, extracted with hot methanol, the alcohol removed and the residue vacuum-distilled. The b.p. was 194-196° at 5 mm and the m.p. 156-158°. The yield was 8.1 g (76%). After recrystallization from methanol, the colorless crystals had m.p. 158-159°.

Found %: N 13.13, 12.97. $C_{12}H_{14}N_2S$. Calculated %: N 12.84.

2-Methyl-4-amino-6,7-tetramethylenebenzthiazole. 6 g of 2-methyl-4-nitro-6,7-tetramethylenebenzthiazole was reduced as described above. The b.p. was 180-181° at 4-5 mm. The yield was 2.8 g (53%). After recrystallization from methanol, the product had m.p. 129-130°.

Found %: N 13.13, 13.17. $C_{12}H_{14}N_2S$. Calculated %: N 12.84.

2-Methyl-5-acetylamino-6,7-tetramethylenebenzthiazole. 1.2 ml of acetic anhydride was added to a solution of 0.4 g of 2-methyl-5-amino-6,7-tetramethylenebenzthiazole in 20 ml of benzene. The precipitate was filtered off and recrystallized from alcohol. The yield was 0.36 g (77%). The white, silky needles had m.p. 232-233°.

Found %: N 10.17, 10.39. $C_{14}H_{16}ON_2S$. Calculated %: N 10.76.

2-Methyl-4-acetylamino-6,7-tetramethylenebenzthiazole. A mixture of 1 g of amine, 25 ml of benzene and 3.2 g of acetic anhydride was boiled for ten hours. The benzene was evaporated and 10 ml of water added to the residue. The precipitate was filtered off and recrystallized from alcohol. The yield was 0.76 g (63%). The white needles had m.p. 164-165°.

Found %: N 10.64, 10.79. $C_{14}H_{16}ON_2S$. Calculated %: N 10.76.

2-Methyl-5-aminobenzthiazole. 100 g of 2-bromo-5-nitroaniline was dissolved in 500 ml of alcohol. To the boiling solution was added a hot solution of sodium disulfide, prepared by dissolving 115 g of sodium sulfide and 18 g of sulfur in 200 ml of alcohol by heating. The mixture was heated on a water bath for one hour, cooled and the dark-red crystals of the sodium salt of 4-nitro-2-aminothiophenol filtered off and dried in air. The yield was 87 g (98%). 122 g of the sodium salt of 4-nitro-2-aminothiophenol was dissolved in 1 liter of water, the solution filtered and 300 ml of acetic anhydride added to it with stirring. To the yellow precipitate was added 500 ml of hydrochloric acid (d 1.19) and the mixture heated on a boiling water bath until the precipitate dissolved completely (two hours). The solution was diluted with water (1:3), cooled and the precipitate filtered off, washed with water and dried. The weight was 66 g and the m.p. 136-137°. Neutralization of the filtrate with ammonia precipitated 6 g of base (m.p. 132°), which had m.p. 137° after recrystallization from alcohol. The total yield was 71 g (56%). The preparation could be used for reduction without further purification.

Into a flask was placed 500 ml of hydrochloric acid (d 1.19) and 100 g of 2-methyl-5-nitrobenzthiazole. The mixture was heated on a water bath to 75° and 100 g of tin sponge added to it in small portions over a period of 2.5 hours with stirring. The mixture was then stirred at 75° for four hours. On the following day the contents of the flask were dissolved in 1050 ml of water and the solution filtered, cooled and neutralized with 950 ml of 30% sodium hydroxide solution, so that the tin salts dissolved completely. The precipitate of amine was filtered off, washed with water, dried and dissolved in 800 ml of methanol, the solution filtered, the alcohol removed and the residue vacuum-distilled. The b.p. was 167-168° at 2-3 mm. The yield was 75 g (89%) and the m.p. 100-102°. According to literature data [5] the m.p. is 102°.

2-Methyl-5-hydroxybenzthiazole. 5 g of 2-methyl-5-aminobenzthiazole was dissolved in 15 ml of water and 2.5 ml of sulfuric acid (d 1.84). The solution was cooled to −10° and diazotized with 2.1 g of sodium nitrite in 4 ml of water at −5°. The diazo solution was gradually introduced dropwise into 800 ml of boiling water. The red precipitate was filtered off, the filtrate extracted with ether, the ether extract dried with potassium carbonate and the ether evaporated; light-yellow crystals were left. The yield was 2 g (40%) and the m.p. 183-187°. After recrystallization from toluene, the substance had m.p. 187°. A mixed melting point with 2-methyl-5-hydroxybenzthiazole, obtained by another method, was not depressed.

2-Methyl-6-hydroxybenzthiazole was prepared similarly. The yield was 30% and the m.p. 157°.

2-Methyl-5-hydroxy-6,7-tetramethylenebenzthiazole. 1.1 g of 2-methyl-5-amino-6,7-tetramethylenebenzthiazole was dissolved in 2 ml of water and 0.35 ml (0.64 g) of sulfuric acid (d 1.84) at 20°. The solution was cooled to −7° and diazotized with 0.36 g of sodium nitrite in 2 ml of water. The diazo solution was introduced into 200 ml of boiling water. The mixture was boiled for 30-40 minutes, cooled and the red precipitate filtered off, washed with water and dried. To free it from coupling products, the base was boiled with 1 ml of benzene and the precipitate filtered off, washed with benzene and recrystallized from alcohol. The yield was 0.6 g (54%), and the m.p. was 255-256°.

Found %: N 6.48, 6.32. $C_{12}H_{13}ONS$. Calculated %: N 6.34.

2-Methyl-5-methoxy-6,7-tetramethylenebenzthiazole. 0.2 g of 2-methyl-5-hydroxy-6,7-tetramethylenebenzthiazole was dissolved in 3 ml of 8% potassium hydroxide. To the solution was added 0.2 ml (0.27 g) of dimethyl sulfate and the mixture stirred for one hour at 20°. After standing, the oil crystallized. The base was filtered off, washed with water, dried, dissolved in benzene and chromatographed on aluminum oxide. The yield was 0.14 g (66%). After recrystallization from benzene, the substance had m.p. 88-89°.

Found %: N 5.78, 5.83. $C_{13}H_{15}ONS$. Calculated %: N 6.00.

Bromo-β-carboxyethylate of 2-methyl-5-metnoxy-6,7-tetramethylenebenzthiazole. A mixture of 0.5 g of 2-methyl-5-methoxy-6,7-tetramethylenebenzthiazole and 0.34 g of β-bromopropionic acid was heated for five hours at 120° and for ten hours at 130°. 1 ml of acetone was added to the mixture, which was boiled on a water bath for ten minutes and the precipitate filtered off and washed with 5 ml of hot acetone. The yield was 0.6 g (73%). The white crystals had m.p. 212-214°.

Found %: Br 20.88, 21.03. $C_{16}H_{20}O_3NSBr$. Calculated %: Br 20.45.

β-Carboxyethyl-p-toluenesulfonate of 2-methyl-5-methoxy-6,7-tetramethylenebenzthiazole. To a hot solution of 0.5 g of the bromo-β-carboxyethylate of 2-methyl-5-methoxy-6,7-tetramethylenebenzthiazole in 10 ml of water was added a warm solution of 0.44 g of silver p-toluenesulfonate in 10 ml of water. The mixture was shaken for 15 minutes and the silver bromide filtered off and washed with 10 ml of water. On standing, the filtrate deposited a white precipitate in a yield of 0.25 g (36%). Evaporation of the filtrate in vacuum yielded 0.05 g of the quaternary salt. The total yield was 0.3 g (43%). The colorless needles had m.p. 116-118°.

Dyes

3,3'-Diethyl-5,5'-dinitro-6,7,6',7'-bis-tetramethylenethiacarbocyanine bromide. A mixture of 0.25 g of 2-methyl-5-nitro-6,7-tetramethylenebenzthiazole and 0.16 g of diethyl sulfate was heated for one hour at 135-140°. To the quaternary salt was added 0.24 g of orthoformic ester and the mixture boiled for 20 minutes. The dye was precipitated with an aqueous solution of potassium bromide and recrystallized from alcohol. The yield was 0.14 g (43%) and the m.p. 220-222°.

Found %: N 8.34, 8.38. $C_{29}H_{31}O_4N_4S_2Br$. Calculated %: N 8.70.

3,3'-Diethyl-4,4'-dinitro-6,7,6',7'-bis-tetramethylenethiacarbocyanine bromide was prepared similarly. After recrystallization from alcohol, the yield was 0.16 g (50%) and the m.p. 262-263°.

Found %: N 8.23, 8.26. $C_{29}H_{31}O_4N_4S_2Br$. Calculated %: N 8.70.

3,3'-Diethyl-5,5'-diacetylamino-6,7,6',7'-bis-tetramethylenethiacarbocyanine perchlorate. After condensation, the dye was precipitated with a hot aqueous solution of sodium perchlorate and recrystallized from alcohol. The yield was 14% and the m.p. 257-259°.

Found %: N 7.88. $C_{33}H_{39}O_6N_4S_2Cl$. Calculated %: N 8.15.

3,3'-Diethyl-4,4'-diacetylamino-6,7,6',7'-bis-tetramethylenethiacarbocyanine perchlorate was obtained similarly to the previous dye. After recrystallization from alcohol, the yield was 8.7% and the m.p. 217° (with decomp.).

Found %: N 7.95. $C_{33}H_{39}O_6N_4S_2Cl$. Calculated %: N 8.15.

3,3'-Diethyl-5,5'-dihydroxy-6,7,6',7'-bis-tetramethylenethiacarbocyanine perchlorate. A mixture of 0.33 g of 2-methyl-5-hydroxy-6,7-tetramethylenebenzthiazole and 0.24 g of diethyl sulfate was heated for three hours at 135-140°. To the warm mass was added 0.32 g of orthoformic ester and 2 ml of dry pyridine and the mixture boiled for 20 minutes. The dye was precipitated with sodium perchlorate. After two recrystallizations from alcohol, the yield was 14% and the m.p. 306-308°.

Found %: N 4.80, 4.92. $C_{29}H_{33}O_6N_2S_2Cl$. Calculated %: N 4.63.

3,3'-Diethyl-5,5'-dihydroxy-6,7,6',7'-bis-tetramethylene-9-methylthiacarbocyanine perchlorate was obtained as above by condensation of the quaternary salt with orthoacetic ester in pyridine with the addition of 2 drops of acetic anhydride. The yield was 13% and the m.p. 219-221°.

Found %: N 4.55, 4.28. $C_{30}H_{35}O_6N_2S_2Cl$. Calculated %: N 4.52.

3,3',9-Triethyl-5,5'-dihydroxy-6,7,6',7'-bis-tetramethylenethiacarbocyanine perchlorate was obtained under similar conditions by condensation of the quaternary salt with orthopropionic ester. After two recrystallizations from alcohol, the yield was 16% and the m.p. 252-253°.

Found %: N 4.52, 4.39. $C_{31}H_{37}O_6N_2S_2Cl$. Calculated %: N 4.42.

3,3'-Diethyl-5,5'-dimethoxy-6,7,6',7'-bis-tetramethylenethiacarbocyanine bromide. A mixture of 0.23 g of 2-methyl-5-methoxy-6,7-tetramethylenebenzthiazole and 0.16 g of diethyl sulfate was heated for three hours at 135-145°. The salt was then converted into the dye in the usual way. The yield was 0.15 g (50%). The green needles with a metallic luster had m.p. 268-269°.

Found %: Br 13.30, 13.05. $C_{31}H_{37}O_2N_2S_2Br$. Calculated %: Br 13.05.

3,3'-Diethyl-5,5'-dimethoxy-6,7,6',7'-bis-tetramethylene-9-methylthiacarbocyanine chloride. To the

quaternary salt, obtained as above, was added 0.24 g of orthoacetic ester, 2 ml of pyridine and two drops of acetic anhydride and the mixture boiled for 20 minutes. The dye was precipitated with ether, the oily precipitate dissolved in 10 ml of alcohol, precipitated with an aqueous solution of potassium chloride and recrystallized from alcohol. The yield was 14% and the m.p. 275-277°.

Found %: Cl 6.40; N 4.79, 4.58. $C_{32}H_{39}O_2N_2S_2Cl$. Calculated %: Cl 6.08; N 4.80.

3,3',9-Triethyl-5,5'-dimethoxy-6,7,6',7'-bis-tetramethylenethiacarbocyanine bromide. The quaternary salt was obtained under analogous conditions and then condensed with orthopropionic ester in pyridine with the addition of two drops of acetic anhydride. After recrystallization from alcohol, the yield was 0.13 g (41%) and the m.p. 269-270°.

Found %: S 9.75, 9.73. $C_{33}H_{41}O_2N_2S_2Br$. Calculated %: S 9.98.

3,3'-Di-(β-carboxyethyl)-5,5'-dimethoxy-6,7,6',7'-bis-tetramethylene-9-ethylcarbocyanine betaine. A mixture of 0.23 g of the β-carboxyethyl-p-toluenesulfonate of 2-methyl-5-methoxy-6,7-tetramethylenebenzthiazole and 0.12 g of orthopropionic ester were dissolved in 1 ml of pyridine and the solution boiled for 30 minutes on a paraffin bath at 120-125°. On the following day, the precipitate filtered off, washed with alcohol, water, several times with boiling alcohol and with ether and dried at 60°. The yield was 13% and the m.p. 206-207°.

Found %: N 4.66, 4.71. $C_{35}H_{40}O_6N_2S_2$. Calculated %: N 4.32.

SUMMARY

1. Several derivatives of 2-methyl-6,7-tetramethylenebenzthiazole were synthesized.

2. A method was developed for replacing an amino group by a hydroxy group through the diazo compound in the benzthiazole series.

3. Quaternary salts and several thiacarbocyanines were prepared from the newly described bases.

4. It was shown that the introduction of hydroxy and methoxy groups into the 5,5'-positions of 6,7,6',7'-bis-tetramethylenethiacarbocyanine produces a bathochromic shift in the absorption maximum by 24 mμ.

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PREPARATION OF 1,6-ANHYDROGLUCOFURANOSE BY THE THERMAL DECOMPOSITION OF CELLULOSE IN VACUUM

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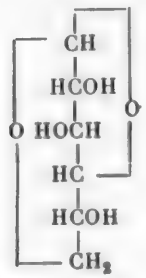
In the present work we continued our study of the chemical composition of the solid distillate obtained by the thermal decomposition of cellulose in vacuum. According to data of previous investigations, the solid distillate, formed from cellulose in 75% yield, consists of 70% levoglucosan and also contains carbonyl compounds, acids, their derivatives (compounds with ester or lactone bonds) and phenols. The use of anionites made it possible to free the levoglucosan from a considerable part of the accompanying substances [1]. As a result of subsequent removal of the levoglucosan by crystallization, we obtained a syrupy product, containing 72% of substances, which showed an increased reducing capacity after hydrolysis, calculated on glucose anhydride, and zero rotation. It was possible to conjecture that together with levoglucosan, the syrupy product contained dextrorotatory substances: 1) polymers of levoglucosan [2] and 2) its isomer, β-1,6-anhydroglucofuranose. The latter was previously isolated from the product of the thermal decomposition of starch in vacuum in about 1% yield [3]. This anhydride had not been obtained from cellulose.



To solve the problem of the presence of polymers, we used the procedure developed by Hurd and Ligett for the analytical separation of mono-, di- and trisaccharides by the vacuum distillation of their propionates [4]. Only the propionate of the monomer was found. The problem of the presence of 1,6-anhydroglucofuranose was solved mainly by the method which was used in the case of the thermal decomposition of starch in vacuum [3]. The neutral residue was acetylated, the acetate vacuum distilled, and the distillate hydrolyzed and freed from levoglucosan by oxidation with periodic acid. 1,6-Anhydroglucofuranose was isolated as the p-nitrobenzoic ester, which was characterized by the specific rotation, the melting point and elementary analysis data. In its properties, the ester obtained was identical with the p-nitrobenzoyl derivative of 1,6-anhydroglucofuranose. Judging by a preliminary calculation from data on the specific rotation of the syrupy product and the amount of glucose anhydrides in it, 1,6-anhydroglucofuranose was formed from cellulose in about 3% yield.

The following considerations may be put forward as regards the mechanism of 1,6-anhydroglucofuranose formation in the thermal decomposition of cellulose in vacuum: 1) under the conditions of the thermal reaction, one cannot exclude the possibility that to a small extent cellulose is hydrolytically cleaved to glucose and the latter is converted into the furanose form with subsequent dehydration; 2) one can postulate that at elevated temperatures, simultaneously with rupture of the 1,4 glucoside bonds, in a very small portion of the elementary units there is rupture of the 1,5 hemiacetal bonds; subsequent isomerization of the fragment formed could lead to β-1,6-anhydroglucofuranose.

EXPERIMENTAL

1. Separation of levoglucosan from the neutral part of the solid distillate. The neutral part of the solid distillate was isolated according to the procedure described previously [1] by successive filtration of an aqueous solution of it through the anionites AN-1 and ÉDÉ-10 and evaporation of the filtrate in vacuum. The product was a white, crystalline substance, which was slightly pasty when ground and had m.p. 100-110°; it contained hydroxyaldehydes and hydroxyketones (positive reaction with Benedict's reagent) and ketones with the grouping of atoms

$-CH_2-CO-CH_2-$ (positive reaction with salicylaldehyde) and had $[\alpha]^{20}D$ −52.8° (c 4; water). The content of reducing substances was 1.33% and the content of substances giving an increase in the reducing capacity, calculated on levoglucosan, was 96.8%. The levoglucosan was isolated from the neutral product either by treatment with anhydrous alcohol in the cold or by recrystallization from 50% alcohol with an additional separation from the mother liquors. After removal of the levoglucosan, the neutral residue was a light-yellow syrup with a small amount of occluded crystals and $[\alpha]^{20}D$ 0°. Its content of reducing substances before hydrolysis was 1.8%, calculated on glucose, and the content of glucose anhydrides was 71.76%. The yield of the residue, calculated on cellulose, was about 8%. The yield of glucose anhydrides in the residue was about 5.5% on the weight of cellulose.

2. Propionylation of the neutral residue and distillation of the propionates. The propionate of the neutral residue was obtained by the usual method by the action of excess propionic anhydride on a solution of the neutral product in anhydrous pyridine. Tenfold amounts of anhydride and pyridine with respect to the weight of the neutral residue were used [5]. The excess reagents were removed by pouring the reaction mixture into 10% sulfuric acid solution, with subsequent extraction of the oil with ether and washing traces of pyridine and acid from the ether solution. From 2 g of neutral residue, we obtained 2.3 g of propionate as a yellow syrup with $[\alpha]^{20}D$ −16.3° (c 4.8; $CHCl_3$). The tripropionate of levoglucosan has $[\alpha]^{20}D$ −56.8° (c 2; $CHCl_3$) [6]. There is no data on the specific rotation of the tripropionate of 1,6-anhydroglucofuranose.

Found %: C 54.57; H 6.65. M 331.6. $C_{15}H_{22}O_8$. Calculated %: C 54.54; H 6.66. M 330.

2.4 g of the propionate of the neutral residue was distilled at $1.3 \cdot 10^{-3}$ mm. It was first established that the propionate of the monomeric glucose anhydride, levoglucosan, boiled at $6.12 \cdot 10^{-2}$ mm at a bath temperature of 170-180°. The propionate of the neutral residue distilled at a bath temperature of 155-182°, mainly at 178-180°, i.e., under the conditions under which the monomer distills. As a result of the beginning of tar formation (due to the slowness of distillation), the residue left in the flask was about 18% of the original propionate. The molecular weight of the residue was 366.7. Consequently, the residue also contained the propionate of the monomer.

3. Identification of 1,6-anhydroglucofuranose in the neutral residue. Treatment of 4 g of the neutral residue with acetic anhydride in pyridine yielded 6.57 g of acetate, which was distilled at 0.5 mm to give two fractions of acetate with the boiling points – 1) 112-140° (2.3 g) and 2) 140-150° (1.86 g). Treatment of the first fraction with a fivefold amount of isopropyl alcohol removed 0.4 g of levoglucosan triacetate from it. A similar treatment of the second fraction did not give positive results. The two fractions were hydrolyzed with a solution of barium methylate in methanol [7] (twofold excess of theoretical) by treatment at room temperature for 24 hours. The reaction mixture was evaporated in vacuum, the residue dissolved in water and the solution freed from Ba^{2+} by the addition of the calculated amount of 0.7 N H_2SO_4. After filtration, the solution was evaporated in vacuum. Hydrolysis gave the following results: first fraction, 1.0 g, $[\alpha]^{20}D$ +8.0°, reducing substances 1.88% and anhydride, 80.42%; second fraction, 0.8 g, $[\alpha]^{20}D$ +4.46°, reducing substances 1.72% and anhydride, 78.57%.

The two fractions were oxidized with periodic acid. Subsequent treatment of the oxidation product (neutralization of the hot solution with barium hydroxide, removal of the barium salts of periodic and iodic acids by filtration, removal as the osazone of the dialdehyde, formed by oxidation of the levoglucosan, freeing the solution of the oxidation product from excess phenylhydrazine by extraction with benzene, evaporation of the solution in vacuum, treatment of the residue with anhydrous alcohol and evaporation of the latter) yielded a syrupy substance. The syrup did not reduce Fehling's solution on boiling, contained 70.6% of glucose anhydride and had $[\alpha]^{20}D$ +30° (c 1.41; water). Assuming that the impurities in the glucose anhydride (about 30%) were optically inactive, the anhydride had $[\alpha]^{20}D$ +42.2° (c 0.945; water). 1,6-Anhydroglucofuranose has $[\alpha]^{20}D$ +43.3° (c 2; water) and m.p. 110.5-111.5° [3].

0.16 g of syrup was treated with p-nitrobenzoyl chloride in pyridine. We obtained 0.48 g (80%) of a crude product with m.p. 222-226°, which was purified by one recrystallization from a mixture of alcohol and acetone (1:2). The m.p. was 235-236° and $[\alpha]^{20}D$ +25.6° (c 0.813; acetone).

Found %: C 52.93; H 3.05; N 6.86. $C_{27}H_{19}O_{14}N_3$. Calculated %: C 53.20; H 3.14; N 6.90.

The p-nitrobenzoyl derivative of D-glucosan $< 1.4 > \beta < 1.6 >$ has m.p. 231-232° and $[\alpha]^{25}D$ +25.3° (c 1.1; acetone [3].

For comparison, the p-nitrobenzoyl ester of levoglucosan, which has not been described previously, was

prepared analogously from 0.324 g of levoglucosan. Two recrystallizations, one from a mixture of alcohol and acetone (1:1) and the second from acetone, yielded 0.5 g of substance. The m.p. was 256-258° and $[\alpha]^{25}D$ −22.1° (c 0.475; acetone).

Found %: N 6.84. $C_{27}H_{19}O_{14}N_3$. Calculated %: N 6.90.

The considerable difference in the specific rotations of p-nitrobenzoates obtained indicated that they were different substances.

SUMMARY

It was shown that the thermal decomposition of cellulose in vacuum formed 1,6-anhydroglucofuranose in a yield of about 3% on the weight of cellulose.

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DIMETHYLAMIDES OF ALKOXYDICHLOROACETIC ACIDS

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The action of phosphorus pentachloride on aliphatic esters of oxamic acid yields amides of alkoxydichloroacetic acids [1] according to scheme (I).

$$NH_2COCOOR + PCl_5 \rightarrow POCl_3 + NH_2COCCl_2OR \quad (I)$$

This reaction is always accompanied by the formation of trichlorophosphazoalkoxydichloroacetyls [2] by scheme (II).

$$NH_2COCCl_2OR + PCl_5 \rightarrow 2HCl + Cl_3P{=}NCOCCl_2OR \quad (II)$$

With esters of dimethyloxamic acid the reaction cannot proceed by scheme (II) and therefore, in the reaction of phosphorus pentachloride with esters of dimethyloxamic acid, one would expect the formation of only the dimethylamides of alkoxydichloroacetic acids by scheme (III).

$$(CH_3)_2NCOCOOR + PCl_5 \rightarrow POCl_3 + (CH_3)_2NCOCCl_2OR \quad (III)$$

Experiment showed that reaction (III) proceeds readily with almost quantitative yields for the methyl, ethyl, n-butyl and isobutyl esters of dimethyloxamic acid.

It was previously found that reaction (I) could not be accomplished with aryl esters of oxamic acid as it proceeded more slowly than reaction (II) [3]. The phenyl ester of dimethyloxamic acid could not react by scheme (II) and therefore it was possible to obtain the dimethylamide of phenoxydichloroacetic acid from it by scheme (III).

The dimethylamides of alkoxydichloroacetic acids and the dimethylamide of phenoxydichloroacetic acid were liquids with a characteristic pleasant smell, somewhat reminiscent of tarragon. They were all soluble in acetone, carbon tetrachloride and benzene and more difficultly soluble in ether and petroleum ether. When treated with water at room temperature, they were slowly hydrolyzed; heating with water produced rapid hydrolysis. The dimethylamide of phenoxydichloroacetic acid was hydrolyzed completely only when boiled with excess sodium hydroxide solution. The chlorine atoms in the dimethylamides of alkoxydichloroacetic acids were extremely labile and were readily replaced by the corresponding groups under the action of alcohols, alcoholates, phenols, ammonia, amines and other compounds, containing labile atoms of hydrogen or metals.

Thermal degradation of the amides of alkoxydichloroacetic acids [3] yielded alkyl halides and oxamyl chloride, which could not be isolated as under the reaction conditions it split out hydrogen chloride and was converted into a tarry mass. Under thermal degradation in vacuum, the dimethylamides of alkoxydichloroacetic acids readily decomposed according to scheme (IV) to give alkyl halides and dimethyloxamyl chloride, which was completely stable under these conditions.

$$(CH_3)_2NCOCCl_2OR \rightarrow RCl + (CH_3)_2NCOCOCl \quad (IV)$$

When the dimethylamides of alkoxydichloroacetic acids were heated slowly in vacuum, they began to decompose at 85-87°, but for the best yields of dimethyloxamyl chloride, the decomposition was best carried out at 85-100°. With the dimethylamides of methoxy- and ethoxydichloroacetic acids, the yield of acid chloride was about 90%. In the case of the dimethylamides of butoxydichloroacetic acids, the yields were considerably less since during the distillation, a considerably larger amount of tarry substances was formed.

When heated above 95° under atmospheric pressure, the dimethylamides of methoxy- and ethoxydichloroacetic acids decomposed with the evolution of almost the theoretical amounts of alkyl halides, but the dimethyloxamyl chloride formed was converted into a thick, dark, tarry mass under these conditions. When heated at atmospheric pressure, the dimethylamides of butoxydichloroacetic acids decomposed at 115-120°.

Dimethyloxamyl chloride was a colorless liquid with a peculiar sharp smell and boiled at 61-63° at 3 mm pressure. It was readily soluble in benzene, dioxane and carbon tetrachloride, somewhat more difficultly in ether and was difficultly soluble in petroleum ether. The structure of dimethyloxamyl chloride was quite rigidly proved by its composition, the preparation method and the chemical properties. When treated with water, it gave a quantitative yield of dimethyloxamic acid, whose properties corresponded to those described in the literature [4]. When treated with ammonia, the dimethyloxamyl chloride gave an 86.0% yield of N,N-dimethyloxamide, whose properties corresponded to those described in the literature [4]. When treated with sodium arylates, dimethyloxamyl chloride gave the previously unknown aromatic esters of dimethyloxamic acid by scheme (V).

$$(CH_3)_2NCOCOCl + NaOAr \rightarrow NaCl + (CH_3)_2NCOCOAr \qquad (V)$$

The phenyl and p-nitrophenyl esters of dimethyloxamic acid were colorless, crystalline substances of a neutral character, which were very slowly hydrolyzed by water at room temperature. In the presence of alkali the hydrolysis proceeded so rapidly that these esters could be titrated with a 0.1 N solution of sodium hydroxide in the presence of phenolphthalein at the same rate as free acids. The same aromatic esters of dimethyloxamic acid were obtained, but in lower yields, from the dimethylamides of methoxy- and ethoxydichloroacetic acids and phenol by the scheme (VI).

$$(CH_3)_2NCOCCl_2OR + C_6H_5OH \rightarrow HCl + RCl + (CH_3)_2NCOCOOC_6H_5 \qquad (VI)$$

EXPERIMENTAL

Only the methyl and ethyl esters of dimethyloxamic acid are described in the literature [5].

Butyl and isobutyl esters of dimethyloxamic acid $C_4H_9OCOCON(CH_3)_2$. With vigorous stirring, a cooled solution of 0.33 mole of dimethylamine in anhydrous ethanol was added to a mixture of 0.3 mole of dibutyl or diisobutyl oxalate and 30 ml of anhydrous ethanol, cooled to 0°. After six hours the ethanol was removed in vacuum and the residue vacuum-distilled on a small column. A second distillation yielded pure esters, which were colorless liquids without an odor, but with a bitter taste. They were miscible with ether, benzene, carbon tetrachloride and acetone, dissolved in alcohol, dissolved with difficulty in petroleum ether and were almost insoluble in water.

The yield of the butyl ester was 70%:

b.p. 94-95° at 3 mm, d^{20}_4 1.0591, $n^{20}D$ 1.1450, MR_D 43.48; calc. 44.75.

Found %: N 8.29. $C_9H_{15}O_3N$. Calculated %: N 8.10.

The yield of the isobutyl ester was 68%:

b.p. 96-98° at 3 mm, d^{20}_4 1.0588, $n^{20}D$ 1.4445, MR_D 43.45; calc. 44.75.

Found %: N 8.91. $C_9H_{15}O_3N$. Calculated %: N 8.10.

Dimethylamides of alkoxydichloroacetic acids. With continuous stirring, 0.1 mole of finely powdered PCl_5 was added to a mixture of 0.1 mole of the appropriate ester of dimethyloxamic acid and 30 ml of CCl_4 and the mixture heated on a water bath at 30°. After 10-15 minutes, the reaction was complete, as indicated by solution of the PCl_5. No gases were evolved during the reaction and the weight of the reaction mixture did not change. After a further 15 minutes, the CCl_4 and $POCl_3$ were distilled off in vacuum at 40° with a receiver cooled to −70°.

Dimethylamides of Alkoxydichloroacetic Acids $ROCCl_2CON(CH_3)_2$

R	Formula	Found						Calculated**		
		%N	%Cl	equiv. after hydrolysis*	d_4^{20}	n_D^{20}	MR_D	%N	%Cl	MR_D
CH_3	$C_5H_9O_2NCl_2$	7.76, 7.71	38.19, 37.97	3.02, 3.07	1.3280	1.4898	40.42	7.53	38.17	40.62
C_2H_5	$C_6H_{11}O_2NCl_2$	6.86, 7.05	35.73, 35.53	2.99, 3.03	1.2630	1.4709	45.06	7.00	35.46	45.24
n-C_4H_9	$C_8H_{15}O_2NCl_2$	—	31.18, 31.27	3.03, 3.05	1.2130	1.4768	53.19	—	31.11	54.46
iso-C_4H_9	$C_8H_{15}O_2NCl_2$	—	30.63, 30.73	3.02, 3.03	1.2250	1.4750	52.40	—	31.11	54.46
C_6H_5	$C_{10}H_{11}O_2NCl_2$	5.72, 5.60	28.09, 28.13	3.04, 3.08***	1.2962	1.5510	60.98	5.65	28.61	61.11

*Using phenolphthalein.

**The calculated equiv. after hydrolysis is 3.00.

***After being boiled for 20 minutes with excess sodium hydroxide solution.

By the usual methods, it was found that the distillate contained 0.0935 mole of $POCl_3$ (93.5%). The residue was the dimethylamide of the corresponding alkoxydichloroacetic acid; the yields were almost quantitative (see table).

Dimethylamide of phenoxydichloroacetic acid. A mixture of 0.01 mole of the phenyl ester of dimethyloxamic acid and 0.0105 mole of finely powdered PCl_5 was placed in a flask connected to a receiver cooled to −70° and heated on an oil bath in a vacuum of 2 mm. The reaction was complete in 20 minutes at 70° and almost the theoretical amount of $POCl_3$ distilled over. The dimethylamide of phenoxydichloroacetic acid remained in the flask as a thick liquid with a characteristic smell; the yield was 99%.

Thermal degradation of dimethylamides of alkoxydichloroacetic acids (by scheme IV). Dimethyloxamyl chloride $(CH_3)_2NCOCOCl$. The dimethylamide of methoxy- or ethoxydichloroacetic acid was distilled in vacuum (3 mm) on an oil bath heated to 115°. After ten minutes the acid chloride began to distill; the temperature in the vapor was 69-70°. The degradation was complete after one hour. In the flask remained 0.5-0.6 g of a viscous tar and the distillate contained dimethyloxamyl chloride. For a final purification, the product was vacuum distilled and had b.p. 61-63° at 3 mm. The yield of the acid chloride from the dimethylamide of methoxydichloroacetic acid was 92% and from the dimethylamide of ethoxydichloroacetic acid, 86.0%.

d^{20}_4 1.2375, $n^{20}D$ 1.4620, MR_D 30.12; calc. 29.50.

Found %: N 10.14, 10.06; Cl 26.13, 26.00. Equiv. after hydrolysis (with phenolphthalein) 2.02, 1.98. $C_4H_6O_2NCl$. Calculated %: N 10.34; Cl 26.17. Equiv. after hydrolysis (with phenolphthalein) 2.00.

Hydrolysis of dimethyloxamyl chloride. To 0.01 mole of dimethyloxamyl chloride was added 1.0 ml of water and the mixture left at room temperature. After 1-2 hours, crystals of dimethyloxamic acid began to precipitate. Excess water was removed by evaporation in vacuum at room temperature. The residue was dimethyloxamic acid (99%). After recrystallization from methanol (2.5 ml to 1.5 g), the long (up to 10 mm), fine needles had m.p. 130-131°, which agrees with literature data [4]. The equivalent and composition of the substance (nitrogen content) corresponded to dimethyloxamic acid.

Reaction of dimethyloxamyl chloride with ammonia. Ammonia was passed for 20 minutes through a solution of 0.05 mole of dimethyloxamyl chloride in 100 ml of C_6H_6. The solution heated up and a voluminous precipitate of ammonium chloride and the reaction product formed. The mixture was heated to boiling and filtered. The precipitate was extracted a second time with 50 ml of boiling benzene. The cooled filtrate deposited N,N-dimethyloxamide (86.0%) with m.p. 102-104°, which agrees with literature data [5]. The nitrogen content of the substance corresponded to that of N,N-dimethyloxamide.

Phenyl ester of dimethyloxamic acid $C_6H_5OCOCON(CH_3)_2$. A. From dimethyloxamyl chloride (by scheme V). To a mixture of 0.02 mole of sodium phenolate and 30 ml of C_6H_6 was added 0.02 mole of dimethyloxamyl chloride with vigorous stirring. The mixture heated up due to the heat of reaction and the form of the precipitate changed. To complete the reaction, the mixture was heated on a water bath for one hour at 55-60°, the sodium chloride was then sucked off (yield 100.00%) and the benzene removed from the filtrate in vacuum. The residue was the crude phenyl ester of dimethyloxamic acid (99.0%) as an almost colorless liquid which crystallized on cooling. For purification, the substance was washed with water (10 x 5 ml) and recrystallized from CCl_4; the yield was 65.0%; the fine, colorless prisms, up to 10 mm in length, had m.p. 75-77°.

Found %: N 7.19, 7.20. Equiv. after hydrolysis (with phenolphthalein) 1.02. $C_{10}H_{11}O_3N$. Calculated %: N 7.26. Equiv. after hydrolysis 1.00.

The phenyl ester of dimethyloxamic acid was readily soluble in methanol, dioxane, acetone and benzene, more difficultly soluble in ether and ethanol, even more difficultly so in carbon tetrachloride and almost insoluble in water and petroleum ether.

B. From the dimethylamide of methoxy- or ethoxydichloroacetic acid (by scheme VI). A mixture of 0.02 mole of the dimethylamide of methoxy- or ethoxydichloroacetic acid and 0.02 mole of phenol was heated for one hour at 70-80°. This liberated 85% of the theoretical amount of HCl and 95% of CH_3Cl or C_2H_5Cl, which were trapped and determined by the usual methods. The flask contained the crude phenyl ester of dimethyloxamic acid as an orange liquid, which rapidly crystallized. The substance was transferred to a filter, washed with water (10 x 5 ml), dried in vacuum and recrystallized twice from CCl_4 (8 ml); the yield was 52.0%; the colorless needles had m.p. 75-77° and did not depress the melting point of phenyl dimethyloxamate obtained from dimethyloxamyl chloride.

p-Nitrophenyl ester of dimethyloxamic acid, $p\text{-}NO_2C_6H_4OCOCON(CH_3)_2$. A mixture of 0.04 mole of sodium p-nitrophenolate, 60.0 ml of dioxane and 0.04 mole of dimethyloxamyl chloride was heated with vigorous stirring on a water bath at 60° for 30 minutes. The mixture was then heated to boiling, the sodium chloride filtered off and the dioxane removed from the filtrate in vacuum. The residue was recrystallized from 50 ml of anhydrous ethanol, when the yield was 65.0%. The p-nitrophenyl ester of dimethyloxamic acid crystallized as colorless, narrow, right-angled prisms, up to 40 mm in length, with m.p. 150-152°.

Found %: N 11.98, 11.90. $C_{10}H_{10}O_5N_2$. Calculated %: N 11.77.

SUMMARY

1. The action of phosphorus pentachloride on aliphatic and the phenyl ester of dimethyloxamic acid gave the dimethylamides of alkoxydichloroacetic acids and the dimethylamide of phenoxydichloroacetic acid.

2. Thermal degradation of the dimethylamides of alkoxydichloroacetic acids yielded dimethyloxamyl chloride.

3. Aromatic esters of dimethyloxamic acid were obtained by the action of sodium arylates on dimethyloxamyl chloride or by the action of phenols on the dimethylamides of alkoxydichloroacetic acids.

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ARYL PHENYLDICHLOROPHOSPHAZOSULFONES

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Recently, A.V. Kirsanov [1] found a reaction by which it was possible to prepare phosphazoacyls by scheme (I).

$$AcNH_2 + PCl_5 \rightarrow 2HCl + AcN{=}PCl_3 \qquad (I)$$

By use of phosphazo reaction (I), A.V. Kirsanov et al. [2] obtained a series of new derivatives of phosphoric acid of the most varied types. However, up to now the phosphazo reaction had not been used for the preparation of true organophosphorus compounds in which the phosphorus atom is attached to a carbon atom. It seemed quite probable that the phosphazo reaction would not only occur with phosphorus pentachloride, but also with alkyl- and arylphosphorus tetrachlorides, dialkyl- and diarylphosphorus trichlorides and trialkyl- and triarylphosphorus dichlorides. Experiment confirmed this hypothesis. The action of phenylphosphorus tetrachloride on amides of aromatic sulfonic acids gave good yields of aryl phenyldichlorophosphazosulfones by scheme (II).

$$ArSO_2NH_2 + C_6H_5PCl_4 \rightarrow 2HCl + ArSO_2N{=}P(C_6H_5)Cl_2 \qquad (II)$$

The aryl phenyldichlorophosphazosulfones were colorless, crystalline substances or thick, viscous liquids, which did not distill in vacuum without decomposition. They were all readily soluble in acetone, toluene, hot benzene and ethyl acetate, difficultly soluble in carbon tetrachloride and insoluble in petroleum ether. The liquid aryl phenyldichlorophosphazosulfones were miscible with diethyl ether, benzene and ethyl acetate.

The aryl phenyldichlorophosphazosulfones reacted readily with amines, alcohols and phenolates. They were hydrolyzed by water at room temperature to arylsulfonamidophenylphosphinic acids.

$$ArSO_2N{=}P(C_6H_5)Cl_2 + 2H_2O \rightarrow 2HCl + ArSO_2NH{-}PC_6H_5(O)OH \qquad (III)$$

Aryl phenyldichlorophosphazosulfones may also be obtained by a second phosphazo reaction (IV), first proposed by Mann and Chaplin [3] and then employed widely for the preparation of various phosphazo compounds [4].

$$ArSO_2NNaCl + C_6H_5PCl_2 \rightarrow NaCl + ArSO_2N{=}P(C_6H_5)Cl_2 \qquad (IV)$$

Reaction (IV) proceeds very vigorously in the absence of solvent and is accompanied by considerable tar formation. However, when a solvent is used it is not possible to obtain pure, crystalline products. Apparently, crystallization is impeded by side products, formed by the action of sodium salts of the chloroamides on the phenyldichlorophosphazo compounds. Phenyl phenyldichlorophosphazosulfone, obtained by scheme (IV), was identified by conversion in 75% yield into the readily crystallizable monomethyl ester of phenylsulfonamidophenylphosphinic acid, which is difficultly soluble in water.

$$C_6H_5SO_2N{=}P(C_6H_5)Cl_2 + 3CH_3ONa \rightarrow 2NaCl + CH_3OCH_3 +$$
$$+ C_6H_5SO_2NNa{-}PC_6H_5(O)OCH_3$$
$$C_6H_5SO_2NNa{-}PC_6H_5(O)OCH_3 + HCl \rightarrow NaCl + C_6H_5SO_2NH{-}PC_6H_5(O)OCH_3$$

Aryl Phenyldichlorophosphazosulfones $ArSO_2N=P(C_6H_5)Cl_2$

Ar	Yield (%)	M.p.	Equiv. after hydrolysis, found	Empirical formula*
C_6H_5	80.0	47—49°	3.98	$C_{12}H_{10}O_2NSPCl_2$
o-$CH_3C_6H_4$	101.0	Viscous oil	3.87	$C_{13}H_{12}O_2NSPCl_2$
p-$CH_3C_6H_4$	101.5	The same	3.85	$C_{13}H_{12}O_2NSPCl_2$
p-ClC_6H_4	102.0	"	3.92	$C_{12}H_9O_2NSPCl_3$
o-$NO_2C_6H_4$	92.5	73—75	3.99	$C_{12}H_9O_4N_2SPCl_2$
m-$NO_2C_6H_4$	92.0	99—100	3.94	$C_{12}H_9O_4N_2SPCl_2$
p-$NO_2C_6H_4$	90.0	171—174	3.99	$C_{12}H_9O_4N_2SPCl_2$
α-$C_{10}H_7$	82.0	99—102	3.94	$C_{16}H_{12}O_2NSPCl_2$
β-$C_{10}H_7$	101.2	Tar	3.94	$C_{16}H_{12}O_2NSPCl_2$

*Calculated equiv.: 4.00.

Thus, there is no doubt that phenyl phenyldichlorophosphazosulfone was obtained by scheme (IV) in more than 75% yield.

The table lists the aryl phenyldichlorophosphazosulfones of the type $ArSO_2N=P(C_6H_5)Cl_2$, obtained by scheme (I).

EXPERIMENTAL

Reaction of aryl sulfonamides with phenylphosphorus tetrachloride. Phenylphosphorus tetrachloride and the corresponding phosphazo compounds react very readily with atmospheric moisture, therefore all operations had to be performed in a dry, inert gas atmosphere.

Equimolecular amounts (0.05 mole) of arylsulfonamide and phenylphosphorus tetrachloride were fused together (70-75°). For the preparation of phenylphosphazo compounds from o- and m-nitrobenzenesulfonamides, the mixture was heated to 100° and with p-nitrobenzenesulfonamide, to 175°. At the given temperatures the reaction proceeded very readily and about 80% of the hydrogen chloride was liberated over a period of 15-20 minutes. To complete the reaction, the mixture was heated for a further 30 minutes. For the determination of the amount of hydrogen chloride liberated, the latter was flushed through with dry carbon dioxide and absorbed in water. From 85-95% of the hydrogen chloride was thus trapped.

In the preparation of p-nitrophenyl phenyldichlorophosphazosulfone, the reaction mixture, which crystallized on cooling, was ground and carefully washed several times with benzene and then with absolute ether. In the preparation of the other phosphazo compounds, the reaction mixtures were uncrystallizable or very difficultly crystallizable, viscous liquids. For the isolation of crystalline phosphazo compounds, the liquid reaction mixture was treated with a small amount of absolute ether. Sometimes the phosphazo compound set to a crystalline mass when the mixture was simply stirred. In the case of the m-nitro derivative, sometimes crystallization only occurred after cooling to −20° and subsequent storage. Phenyl phenyldichlorophosphazosulfone was comparatively readily soluble in ether at room temperature and therefore it was crystallized from concentrated solutions with cooling. The crystallized phosphazo compounds were sucked off and washed several times with ether. The crystalline phosphazo compounds obtained in this way were quite pure substances, suitable for further syntheses. Where required, they could be recrystallized from ether, ethyl acetate or another suitable solvent, but the melting points of the recrystallized products were raised by only 2-3°. The table gives the yields, melting points and titration data of unrecrystallized products. The liquid phosphazo compounds were obtained in a less pure state, since they could not be distilled in vacuum (at 1 mm) without decomposition.

Preparation of phenyl phenyldichlorophosphazosulfone from phenyldichlorophosphine and the sodium salt of benzenesulfonochloramide. With cooling and stirring, an equimolecular amount of the dry sodium salt of the

chloramide was added in small portions to a solution of 0.05 mole of phenyldichlorophosphine in 30 ml of dry benzene. The reaction proceeded very vigorously. The reaction mixture was heated to boiling for 15 minutes and poured into 200 ml of dry benzene. The precipitated sodium chloride was filtered off and the filtrate evaporated in vacuum on a water bath. The residue was a colored, uncrystallizable liquid. The yield was 89.8%.

Found: equiv. after hydrolysis 3.95. $C_{12}H_{10}O_2NSPCl_2$. Calculated: equiv. after hydrolysis 4.00.

Preparation of monomethyl ester of phenylsulfonamidophenylphosphinic acid. Into a three-necked flask, fitted with a reflux condenser, a stirrer and a dropping funnel, was placed 10 ml of anhydrous methyl alcohol and 0.01 g-at. of sodium. When the sodium had dissolved, a solution of 0.003 mole of phenyl phenyldichlorophosphazosulfone in 10 ml of benzene was added dropwise with vigorous stirring. The mixture was heated for 0.5 hours at 50° and then the benzene and alcohol were removed in vacuum on a water bath. The dry residue was dissolved in 10 ml of water and acidified with hydrochloric acid. The monomethyl ester precipitated was separated and washed well with water. It was purified by recrystallization from 50% alcohol. The yield was 75% and the m.p. 172-173°.

Found %: OCH_3 9.91. Equiv. 1.02. $C_{13}H_{14}O_4NSP$. Calculated %: OCH_3 9.97. Equiv. 1.00.

SUMMARY

The action of phenylphosphorus tetrachloride on aryl sulfonamides yielded aryl phenyldichlorophosphazosulfones.

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SYNTHESES WITH COMPLEX COMPOUNDS

IV. PREPARATION OF PHENOLINDOPHENOL-3,3'-DICARBOXYLIC ACID

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The presence, under appropriate conditions, of so-called intramolecular dissociation in cyclic salts may have a substantial effect on their reactivity [1, 2]. In comparison with the compounds forming them, such cyclic salts may have an increased or even qualitatively new reactivity. The behavior of the cyclic aluminum salt of salicylic acid, described in the present article, will serve as an example of the latter case. Under the action of dilute nitric acid, salicylic acid itself or sodium salicylate do not form the same products as are given by cyclic aluminum salicylate.

When a mixture of salicylic acid and aluminum nitrate was heated, the reaction mixture acquired an intense blue color. The intensity of the color developed to the greatest extent when the amount of aluminum nitrate was not less than a fourfold excess, with respect to salicylic acid. It was also strongly dependent on the concentration and the optimal was when there was 8-10 times the amount of water as salicylic acid. The pH of the reaction mixture, the temperature and heating time were of considerable importance. The best results were obtained with a heating period of 4-5 minutes at 100°. Cooling the reaction mixture and acidifying it with hydrochloric acid yielded the colored substance formed during the reaction and it was found to be phenolindophenol-3,3'-dicarboxylic acid in 56% yield. This was the first time it had been prepared. Besides phenolindophenol-3,3'-dicarboxylic acid, the reaction mixture also yielded hydroquinonecarboxylic and 5-nitrosalicylic acids in 12 and 10% yields, respectively.

The formation of several products indicated that the reaction was complex. The hydroquinonecarboxylic acid was isolated by ether extraction of the acidified filtrate after separation of the phenolindophenol-3,3'-dicarboxylic acid and reduction with zinc dust. For isolation of the 5-nitrosalicylic acid, the reaction mixture was acidified and extracted with ether, the extract evaporated to dryness, the residue dissolved in alcohol and freed from phenolindophenol-3,3'-dicarboxylic acid with activated charcoal, the charcoal separated by filtration, the filtrate evaporated to dryness, the residue dissolved in 1 N sodium hydroxide solution and the 5-nitrosalicylic acid precipitated from the solution by acidification with concentrated hydrochloric acid.

Data obtained in the study of this reaction made it possible to put forward the following preliminary hypotheses on a possible reaction mechanism. The first stage is the formation of the cyclic aluminum salt of salicylic acid, which is described in the literature [3].

Due to intramolecular dissociation [1, 2], this cyclic salt has an increased reactivity [4].* As a result of

*The structure of the cyclic aluminum salt, showing intramolecular dissociation, is represented here in accordance with the symbolism recommended previously [1, 2].

The crossed-out, dotted line denotes that the structure presented should not be understood as one in which the oxygen atom of the phenol group is completely ionized. The bond between this oxygen atom and the aluminum atom has only a partial ionic character, which, however, has a considerable effect on the course of the reaction examined.

this, it is readily oxidized by the nitric acid liberated during its formation, probably to hydroquinonecarboxylic acid with the simultaneous reduction of the nitric to nitrous acid.

The formation of hydroquinonecarboxylic acid was confirmed by its isolation from the reaction mixture. It is known that hydroquinonecarboxylic acid is also formed in the oxidation of salicylic acid by certain other oxidants. In particular, one of the methods of preparing hydroquinonecarboxylic acid consists of the oxidation of salicylic acid with persulfate [5]. The formation of nitrous acid in the reaction mixture was also demonstrated by passing a stream of air through the latter and then passing the emergent gases through sodium hydroxide solution, which was afterward found to contain large amounts of nitrite.

As was recently shown [4], the nitrous acid formed in the reaction mixture reacts with the cyclic aluminum salt of salicylic acid, giving the corresponding nitroso compound.

Nitrosation of the cyclic salts, showing intramolecular dissociation, proceeds more readily than with free salicylic acid. This increased reactivity of such cyclic salts of salicylic acid, with respect to nitrosation, was recently noted in the literature [4, 6].

The nitroso compound formed then reacts with the remaining unchanged cyclic aluminum salt of salicylic acid, leading to the cyclic aluminum salt of phenolindophenol-3,3'-dicarboxylic acid.

This reaction course is possible in view of the smooth formation of the cyclic aluminum salt of phenolindophenol-3,3'-dicarboxylic acid by the direct addition of the cyclic aluminum salt of salicylic acid to the cyclic aluminum salt of 5-nitrososalicylic acid, obtained in accordance with [4].

The formation of 5-nitrosalicylic acid in the reaction mixture occurs as a result of partial oxidation of 5-nitrososalicylic acid. The formation of 5-nitrosalicylic acid by the reaction of salicylic acid with nitrous acid in an acid medium has been known for a long time [7].

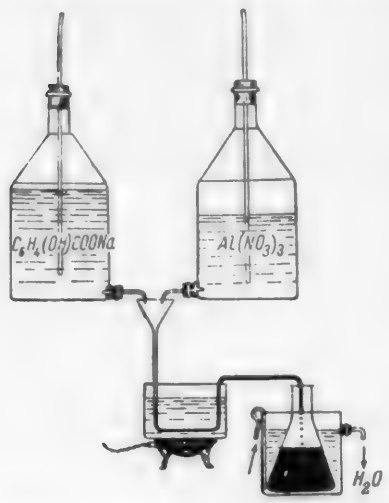
In the given reaction, the aluminum nitrate may be replaced by mixtures of equivalent amounts of aluminum chloride or sulfate and sodium nitrate. Instead of aluminum nitrate it is possible to use the nitrates of certain other elements, which react with salicylic acid to give cyclic salts, capable of intramolecular dissociation under the reaction conditions. Thus, for example, the formation of phenolindophenol-3,3'-dicarboxylic acid proceeds just as successfully with the use of chromium, zirconium, thorium and gallium nitrates as in the case of aluminum nitrate. Beryllium and zinc nitrates are slightly less effective.

EXPERIMENTAL

Preparation of phenolindophenol-3,3'-dicarboxylic acid. 1. Synthesis of small amounts. 2.5 g of salicylic acid was placed in a flask of about 100-ml capacity, 20 ml of water and 1.5 g of crystalline sodium acetate added and the mixture heated on a boiling water bath. Then 10 g of aluminum nitrate was added and the mixture stirred vigorously on a boiling water bath for 4-5 minutes. The reaction mixture was cooled and 25 ml of dilute hydrochloric acid (1:1) added. The color of the solution rapidly changed from intense blue to violet and, finally, to red. The phenolindophenol-3,3'-dicarboxylic acid thus liberated collected into coarse lumps, which were filtered off, washed with water and recrystallized from 20-25% alcohol. Ether extraction of the strongly red filtrate yielded a certain amount of extra phenolindophenol-3,3'-dicarboxylic acid. The total yield of phenolindophenol-3,3'-dicarboxylic acid was 56%, calculated on the salicylic acid.

2. Synthesis of large amounts. For the preparation of large amounts of phenolindophenol-3,3'-dicarboxylic

acid, it was convenient to work with a continuous apparatus (see figure). Into one Mariotte bottle was placed a solution of 500 g of $Al(NO_3)_3 \cdot 9H_2O$ in 250 ml of water. 17 ml of conc. H_2SO_4 added, the solution stirred well and the flow rate from the bottle adjusted to 1 ml/min. Into the other Mariotte bottle was placed a solution containing 160 g of sodium salicylate in 750 ml of water and the flow rate adjusted to 1.5 ml/min. The two solutions, flowing at the given rates, were led into a bent glass tube, of 10-mm internal diameter, placed in a boiling water bath in such a way that a 10-cm length of the tube was in the boiling water. The dark-colored solution of the cyclic aluminum salt of phenolindophenol-3,3'-dicarboxylic acid formed flowed continuously from the other end of the tube. Naturally, it is possible to use other flow rates of the mixed solution, provided that the dimensions of the part of the apparatus immersed in the boiling bath are changed in such a way that the time that the reaction mixture is in the heated zone is 4-5 minutes. The solution issuing from the reaction tube was led into a receiver, cooled externally with water. The phenolindophenol-3,3'-dicarboxylic acid was isolated from the solution obtained by acidification with hydrochloric acid and salting out with sodium chloride.



Continuous apparatus for the preparation of large amounts of phenolindophenol-3,3'-dicarboxylic acid.

The phenolindophenol-3,3'-dicarboxylic acid was a dark-red powder melting at 305° (with decomp.).

Found %: C 62.37; H 2.95; N 4.52. $C_{14}H_9O_6N$. Calculated %: C 62.22; H 2.88; N 4.44.

The substance dissolved readily in alcohol and acetone and less readily in ether, benzene, chloroform and carbon tetrachloride, forming solutions with colors from yellow to red-orange. It was sparingly soluble in water and the orange aqueous solutions had a light-absorption maximum at 380 mμ and a molar absorption coefficient of $2.9 \cdot 10^4$. When a weakly acid or a neutral aqueous solution was treated with salts of Zr, Th, Al, Ga, Cu and also certain other elements, the orange color became blue.

Preparation of 4,4'-dihydroxydiphenylamine-3,3'-dicarboxylic acid. 1.4 g of phenolindophenol-3,3'-dicarboxylic acid was dissolved in 30 ml of 2 N NaOH solution, 5 g of sodium hydrosulfite added and the mixture heated to 50-60°. After complete reduction (indicated by the solution color changing from blue to brown), the reaction mixture was made just acid to congo with conc. HCl and extracted with ether. The ether extract was evaporated to dryness, the residue dissolved in 50 ml of alcohol, a small amount of activated charcoal added, the solution filtered and the filtrate evaporated in vacuum. Recrystallization from aqueous alcohol gave a light, brownish-yellow product with m.p. 246°.

Found %: C 61.95; H 3.72; N 4.36. $C_{14}H_{11}O_6N$. Calculated %: C 61.83; H 3.81; N 4.42.

The substance was readily soluble in alcohol and acetone and less so in ether. It was almost insoluble in water. It dissolved readily in solutions of ammonia, soda and bicarbonate to give light, brownish solutions. Alkaline solutions were readily oxidized under the action of atmospheric oxygen and changed to an intense blue. 4,4'-Dihydroxydiphenylamine-3,3'-dicarboxylic acid was not oxidized in acid solutions by atmospheric oxygen, but was readily oxidized by cupric and thallic salts and a series of other oxidants.

SUMMARY

Heating salicylic acid with an aqueous solution of aluminum nitrate formed the aluminum salt of phenolindophenol-3,3'-dicarboxylic acid, giving the solution an intense blue color. After acidification of the reaction mixture, it was possible to isolate free phenolindophenol-3,3'-dicarboxylic acid, reduction of which gave 4,4'-dihydroxydiphenylamine-3,3'-dicarboxylic acid. The properties of the compounds obtained are described and a hypothesis is put forward on the reaction mechanism.

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SYNTHESIS OF DIALKYLAMINOALKYL DERIVATIVES OF INDAZOLE

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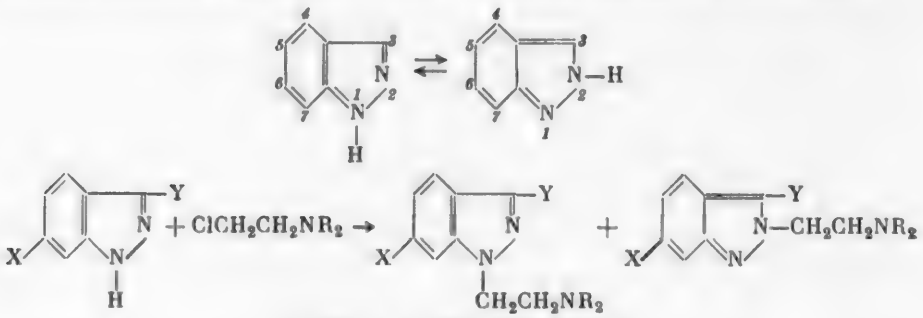
The purpose of this work was the synthesis of dialkylaminoalkyl derivatives of indazole for a study of the chemical properties and pharmacological and antibacterial investigations. It is known that the dialkylaminoalkyl grouping has considerable value in drugs. Many antihistaminics, spasmolytics, local anesthetics, antimalarials and certain other drugs contain this grouping connected to a nitrogen or an oxygen atom. Therefore, it seemed interesting to prepare compounds of this type in the indazole series, which may be regarded as isosters of indole and isomers of benzimidazole, heterocycles, forming part of the molecules of a series of biologically important substances.

N-Diethylaminoethyl-6-nitroindazole was synthesized in good yield by the condensation of 6-nitroindazole with diethylaminoethyl chloride in the presence of sodium alcoholate. N-Dimethylaminoethyl-6-nitroindazole, N-dimethylaminoethyl-3-chloroindazole and N-dimethylaminoethylindazole were prepared analogously. Since the free base of dimethylaminoethyl chloride polymerizes readily on distillation, its hydrochloride and twice the amount of alcoholate were used in the reaction. In the case of indazole, the yield was somewhat lower than for 6-nitro- and 3-chloroindazole. This may be explained by the fact that the presence of a chlorine or a nitro group draws off the electrons promoting the increased activity of the hydrogen atom at the nitrogen.



X = NO_2, H R = CH_3, C_2H_5; Y = Cl, H

As in the alkylation of indazole and its derivatives [1], in their condensation with dialkylaminoalkyl chlorides, the 1- and 2-substituted derivatives were formed. We separated the isomers by different methods: 1- and 2-diethylaminoethyl-6-nitroindazole were separated by fractional crystallization of the hydrochlorides from ethyl alcohol and 1- and 2-dimethylaminoethyl-6-nitroindazole, by fractional precipitation with picric acid. It was possible to obtain only one isomer in a pure form by fractional crystallization of the hydrochlorides of 1- and 2-dimethylaminoethyl-3-chloroindazoles. We were able to isolate the two isomers by preparing and recrystallizing the hydrochlorides in a series of solvents – ethyl acetate, ethyl alcohol, isopropyl alcohol and acetone; the 1- and 2-isomers of dimethylaminoethylindazole were separated by an analogous method. With hydrogen chloride, 1-dimethylaminoethylindazole gave a monohydrochloride and the 2-isomer, a dihydrochloride. The picrates of the two isomers differed considerably in melting point.

In the N-alkylaminoalkylation of 6-nitroindazole and indazole, the 2-isomers were formed predominantly, while in the case of 3-chloroindazole, the 1-isomer was the main product.

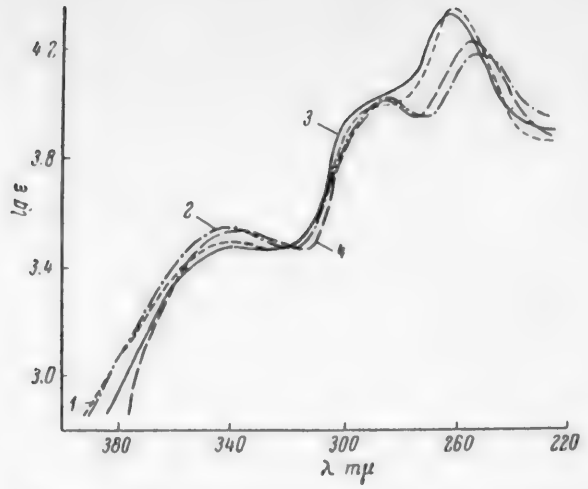


Fig. 1. Ultraviolet absorption curves: 1) 1-diethylaminoethyl-6-nitroindazole; 2) 1-methyl-6-nitroindazole; 3) 2-diethylaminoethyl-6-nitroindazole; 4) 2-methyl-6-nitroindazole.

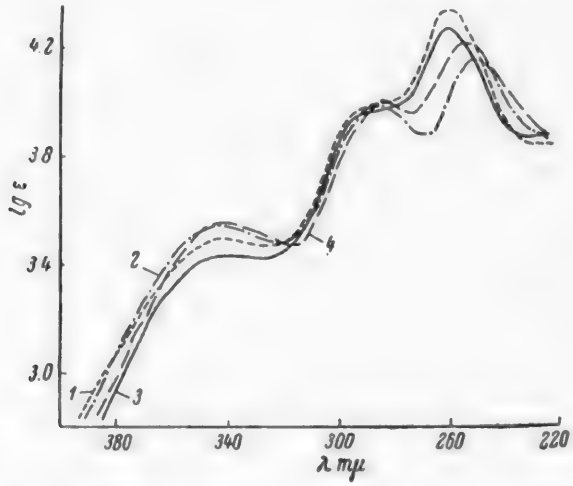


Fig. 2. Ultraviolet absorption curves: 1) 1-dimethylaminoethyl-6-nitroindazole; 2) 1-methyl-6-nitroindazole; 3) 2-dimethylaminoethyl-6-nitroindazole; 4) 2-methyl-6-nitroindazole.

The chemical method is only suitable for proving the structure of indazole derivatives in separate cases [2]. Although Auwers et al. [3] obtained good results in this direction by refractometric investigations, the determination of the ultraviolet absorption spectra was found to be more convenient [4]. The structures of all the isomeric compounds we obtained were proved by comparison of their ultraviolet absorption spectra with the spectra of the corresponding 1- and 2-methyl derivatives of indazole. The results obtained were confirmed by chemical conversions. Thus, by replacement of the chlorine by hydrogen by means of hydriodic acid and red phosphorus, the compound identified as 1-dimethylaminoethyl-3-chloroindazole by the spectral method was converted into 1-dimethylaminoethylidazole. The spectral curves are presented in Figs. 1-4.*

N-Dialkylaminoethyl-6-aminoindazoles were obtained from the corresponding nitro derivatives by hydrogenation in the presence of Raney nickel. It is interesting to note that 6-aminoindazole was obtained by Kwartler and Lucas [5] by hydrogenation of 6-nitroindazole in the presence of a large amount of Raney nickel at 30-40 atmos pressure of hydrogen at 50°, while we showed that N-dialkylaminoethyl-6-nitroindazoles were hydrogenated very readily and rapidly at room temperature and atmospheric pressure.

6-Hydroxyindazole could be obtained from 6-aminoindazole by diazotization and subsequent heating of the diazonium salt with sulfuric acid [6]. The compound obtained in this way was difficult to purify. According to the data of Davies [7] and other authors, the hydrolysis of 6-aminoindazole with dilute sulfuric acid at an elevated temperature in an autoclave gives 6-hydroxyindazole in good yield. We found that the hydrolysis of a mixture of 1- and 2-diethylaminoethyl-6-aminoindazoles with 10% sulfuric acid at 160-180° for 20 hours gave only 2-diethylaminoethyl-6-hydroxyindazole; the 1-diethylaminoethyl-6-aminoindazole was recovered unchanged.

Chlorination of N-dialkylaminoethyl-6-nitroindazoles with the calculated amount of chlorine in water at 40-50° led to the formation of monochloro derivatives. In analogy with the chlorination of indazole [3] and 6-nitroindazole [7], it can be considered that the chlorine atom entered the ring at position 3.

For a pharmacological study it was interesting to prepare quaternary salts of indazole derivatives, since it is known that a series of quaternary ammonium salts have a high biological activity. We prepared the quaternary salts of trialkylaminoethylindazoles (I) and (II) by the usual method, namely, the reaction of N-dialkylaminoethyl derivatives of indazole with methyl iodide in benzene solution without heating or without solvent at

*The spectra were plotted in the physical-chemistry laboratory of the All-Union Scientific-Research Institute on Chemical Pharmaceutics under the direction of Yu.N. Sheinker, whom the authors would like to thank.

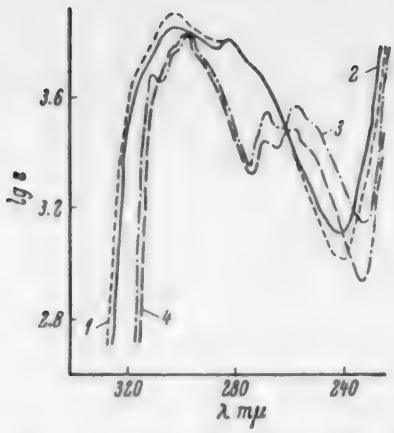


Fig. 3. Ultraviolet absorption curves: 1) 2-methyl-3-chloroindazole; 2) 2-dimethylaminoethyl-3-chloroindazole; 3) 1-methyl-3-chloroindazole; 4) 1-dimethylaminoethyl-3-chloroindazole.

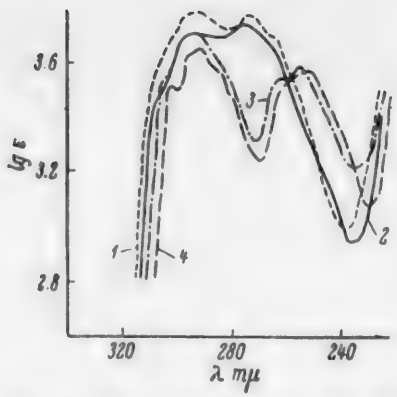
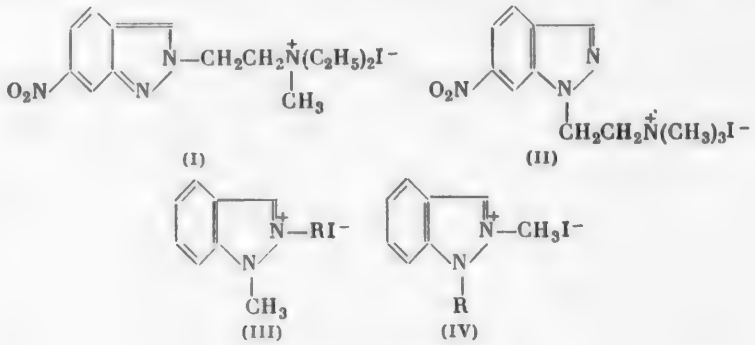


Fig. 4. Ultraviolet absorption curves: 1) 2-methylindazole; 2) 2-dimethylaminoethylindazole; 3) 1-methylindazole; 4) 1-dimethylaminoethylindazole.

100° in a sealed tube. This produced the addition of only one molecule of methyl iodide, despite the difference in the reaction conditions. Apparently, the initially formed quaternary nitrogen, which attracts electrons strongly, lowers the activity of the nitrogen atoms close to it, preventing their reaction with methyl iodide [8]. This may probably explain why, for example, alkylindazoles [9] and alkylnitroindazoles [10] react with only one molecule of methyl iodide, although the quaternary salt formed contains a further tertiary nitrogen, (III) and (IV).



EXPERIMENTAL

1- and 2-Diethylaminoethyl-6-nitroindazoles. With stirring, 16.3 g of 6-nitroindazole and 70 ml of anhydrous alcohol were added to the alcoholate obtained from 2.53 g of sodium and 80 ml of anhydrous alcohol. To the dark-red solution was added 15.6 g of freshly distilled diethylaminoethyl chloride in 25 ml of anhydrous alcohol, after which the mixture was boiled with stirring for five hours. The precipitate of sodium chloride was filtered off and washed with anhydrous alcohol, the alcohol solution evaporated and the residual oil heated in vacuum on a boiling water bath for half an hour and then dissolved in 60 ml of 10% hydrochloric acid. The unreacted 6-nitroindazole was extracted from the acid solution with ether. With cooling, a concentrated solution of sodium hydroxide was added to the aqueous layer and the alkaline solution extracted with ether. The ether solution was dried and evaporated. We obtained 24.85 g (94.9%) of a yellow, oily substance, a mixture of 1- and 2-diethylaminoethyl-6-nitroindazoles. For separation of the isomers, a solution of them in 180 ml of anhydrous alcohol was cooled and treated with a saturated alcohol solution of hydrogen chloride to an acid reaction to congo, the mixture heated with charcoal and the solution filtered and cooled. We obtained 24.35 g of a mixture of the hydrochlorides of the two isomers with m.p. 152-178°; six recrystallizations from alcohol yielded the

hydrochloride of 2-diethylaminoethyl-6-nitroindazole as yellow prisms with m.p. 192-193°, which were readily soluble in water, more difficultly so in alcohol and acetone and insoluble in ether. The free base, isolated from the hydrochloride, had m.p. 33-34°.

Found %: N 18.52, 18.94; Cl 12.17. $C_{13}H_{19}O_2N_4Cl$. Calculated %: N 18.75; Cl 11.87.

The first two alcohol mother solutions were combined and evaporated; four recrystallizations of the residue from alcohol yielded the hydrochloride of 2-diethylaminoethyl-6-nitroindazole as yellow crystals with m.p. 168-169°, which were very readily soluble in water, more difficultly so in alcohol and acetone and insoluble in ether.

Found %: N 18.58; Cl 12.12. $C_{13}H_{19}O_2N_4Cl$. Calculated %: N 18.75; Cl 11.87.

1- and 2-Dimethylaminoethyl-6-nitroindazoles. A mixture of 1- and 2-dimethylaminoethyl-6-nitroindazoles was obtained in 81.7% yield under the conditions of the previous experiment by condensation of 6-nitroindazole with dimethylaminoethyl chloride. For separation of the isomers, a solution of the mixture obtained (19.15 g) in 95 ml of alcohol was treated with a solution of 18.8 g of picric acid in 470 ml of alcohol in ten portions and the picrate precipitates were collected separately. The first four portions were combined and treated with conc. HCl; after separation of the picric acid, the aqueous solution was washed with ether and evaporated to dryness in vacuum. Recrystallization of the residue from alcohol yielded the pure hydrochloride of 2-dimethylaminoethyl-6-nitroindazole as yellow platelets with m.p. 207-208°, which were readily soluble in water, more difficultly so in alcohol and acetone and insoluble in ether. The free base, isolated from the hydrochloride, had m.p. 82-83°.

Found %: N 20.70; Cl 13.11. $C_{11}H_{15}O_2N_4Cl$. Calculated %: N 20.70; Cl 13.10.

Similarly, the last three portions of picrate yielded the hydrochloride of 1-dimethylaminoethyl-6-nitroindazole as light-yellow needles with m.p. 235-236°, which were readily soluble in water, more difficultly so in alcohol and acetone and insoluble in ether. The free base, isolated from the hydrochloride, had m.p. 40-41°.

Found %: N 21.01; Cl 13.08. $C_{11}H_{15}O_2N_4Cl$. Calculated %: N 20.70; Cl 13.10.

1- and 2-Dimethylaminoethyl-3-chloroindazoles. To the solution of alcoholate, obtained from 6.44 g of metallic sodium and 180 ml of anhydrous alcohol, was added 15.25 g of 3-chloroindazole and 100 ml of anhydrous alcohol with stirring and then 20.16 g of dimethylaminoethyl chloride hydrochloride in 300 ml of anhydrous alcohol, after which the mixture was boiled for five hours. The sodium chloride precipitate was filtered off and washed with anhydrous alcohol, the alcohol solution evaporated and the residual oil heated in vacuum on a boiling water bath for half an hour and then dissolved in 120 ml of 5% hydrochloric acid. The unreacted 3-chloroindazole was extracted from the acid solution with ether. The aqueous solution was then made alkaline with sodium hydroxide solution and extracted with ether. The ether solution was dried and evaporated. We obtained 19.36 g (86.6%) of a light-yellow, oily substance, a mixture of 1- and 2-dimethylaminoethyl-3-chloroindazoles. For separation of the isomers, with cooling a solution of the oil obtained in 200 ml of ethyl acetate was treated with a saturated alcohol solution of hydrogen chloride to an acid reaction to congo. The precipitate was collected and after three recrystallizations from alcohol, it yielded the hydrochloride of 1-dimethylaminoethyl-3-chloroindazole as colorless prisms with m.p. 179-180°, which were readily soluble in water, more difficultly so in alcohol and acetone and insoluble in ether.

Found %: C 50.28; H 5.92; N 16.07, 16.29. $C_{11}H_{15}N_3Cl_2$. Calculated %: C 50.78; H 5.81; N 16.15.

The ethyl acetate mother solution was evaporated to dryness; three recrystallizations of the residue from acetone yielded the hydrochloride of 2-dimethylaminoethyl-3-chloroindazole as colorless plates with m.p. 158.5-159°, which were readily soluble in water, more difficultly so in alcohol and acetone and insoluble in ether.

Found %: C 50.74; H 5.93; N 16.17. $C_{11}H_{15}N_3Cl_2$. Calculated %: C 50.78; H 5.81; N 16.15.

1- and 2-Dimethylaminoethylindazoles. A mixture of 1- and 2-dimethylaminoethylindazoles was obtained as an almost colorless oil in 67% yield similarly to the preparation of the 3-chloro derivatives. For separation of the isomers, 2 g of the mixture was dissolved in 45 ml of ethyl acetate and a saturated alcohol solution of hydrogen chloride added to the solution with cooling until the reaction was acid to congo. The precipitate was collected; after three recrystallizations from isobutyl alcohol, the substance had m.p. 171-181°. The melting point did not change with further recrystallization. The dihydrochloride of 2-dimethylaminoethylindazole formed hygroscopic, colorless prisms, which were readily soluble in alcohol.

Found %: N 16.00; Cl 26.96. $C_{11}H_{17}N_3Cl_2$. Calculated %: N 16.03; Cl 27.05.

Treatment of the dihydrochloride with picric acid in alcohol solution yielded the picrate of 2-dimethylaminoethylindazole as yellow platelets with m.p. 235° (with decomp.), which were soluble in acetone and more difficultly so in alcohol.

Found %: C 48.83; H 4.40; N 20.37. $C_{17}H_{18}O_7N_6$. Calculated %: C 48.81; H 4.34; N 20.09.

The oxalate formed colorless crystals (from anhydrous alcohol) with m.p. 154-156° (with decomp.).

Found %: C 55.82; H 6.23; N 14.73. $C_{13}H_{17}O_4N_3$. Calculated %: C 55.90; H 6.14; N 15.05.

1-Dimethylaminoethylindazole. a) The ethyl acetate mother solution, after separation of the hydrochloride of the 2-substituted isomer, was evaporated to dryness; after two recrystallizations from isobutyl alcohol, the residue yielded the hydrochloride of 1-dimethylaminoethylindazole as colorless platelets with m.p. 143-144°, which were readily soluble in water, more difficultly so in alcohol and acetone and insoluble in ether.

Found %: C 58.66; H 7.15; N 18.40. $C_{11}H_{16}N_3Cl$. Calculated %: C 58.53; H 7.14; N 18.62.

Treatment of the hydrochloride with an alcohol solution of picric acid yielded a picrate as yellow prisms with m.p. 169-170°, which were soluble in acetone.

Found %: C 48.99; H 4.50; N 20.34. $C_{17}H_{18}O_7N_6$. Calculated %: C 48.81; H 4.34; N 20.09.

b) A mixture of 1.3 g of 3-chloro-1-dimethylaminoethylindazole, 1 g of red phosphorus and 6 ml of hydriodic acid (d 1.7) was boiled for 24 hours. At the end of the reaction, the solution was filtered free from excess phosphorus, diluted with 50 ml of water and evaporated to 20 ml and then the residue was made alkaline with sodium hydroxide and extracted with ether. The ether solution was dried and evaporated; we obtained 0.83 g (81.4%) of a colorless oil, from which a hydrochloride with m.p. 143-144° was obtained. A mixed melting point with the hydrochloride of 1-dimethylaminoethylindazole obtained by method "a" was not depressed. The picrate had m.p. 169-170°. A mixed melting point with the picrate obtained by method "a" was not depressed.

1-Diethylaminoethyl-6-aminoindazole. A solution of 1.32 g of 1-diethylaminoethyl-6-nitroindazole in 20 ml of methyl alcohol was hydrogenated in the presence of 0.5 g of Raney nickel at room temperature and atmospheric pressure. The solution was filtered free from catalyst and evaporated; we obtained 1.07 g (92.2%) of a dark, oily substance. Treatment with picric acid in an alcohol solution yielded a picrate with m.p. 160-161°; after recrystallization from alcohol, the fine, yellow prisms had m.p. 161-162° and were soluble in acetone, more difficultly so in alcohol and insoluble in benzene and ether.

Found %: C 49.95, 49.08; H 5.27, 5.02; N 21.02. $C_{13}H_{23}O_7N_7$. Calculated %: C 49.46; H 5.02; N 21.25.

2-Diethylaminoethyl-6-aminoindazole was obtained similarly to 1-diethylaminoethyl-6-aminoindazole in 94% yield. The picrate formed red prisms with m.p. 127.5-128° (from alcohol), which were readily soluble in acetone, more difficultly so in alcohol and insoluble in benzene and ether.

Found %: C 49.27; H 4.92; N 21.30. $C_{13}H_{23}O_7N_7$. Calculated %: C 49.46; H 5.02; N 21.25.

1-Dimethylaminoethyl-6-aminoindazole was obtained similarly to the previous compound in 96.5% yield. It appeared as colorless prisms (from benzene) with m.p. 71-72°, which were readily soluble in ether, benzene, alcohol and acetone, more difficultly so in water and insoluble in petroleum ether.

Found %: C 64.48; H 8.02; N 27.16. $C_{11}H_{16}N_4$. Calculated %: C 64.68; H 7.90; N 27.43.

2-Dimethylaminoethyl-6-aminoindazole was obtained similarly to 1-dimethylamino-6-aminoindazole in 98.5% yield. It appeared as colorless plates with a pinkish tinge, had m.p. 91-91.5° and was readily soluble in alcohol, acetone, water and benzene and insoluble in petroleum ether.

Found %: C 64.57; H 7.89; N 27.35. $C_{11}H_{16}N_4$. Calculated %: C 64.68; H 7.90; N 27.43.

6-Hydroxy-2-diethylaminoethylindazole. A mixture of 6.96 g of 1- and 2-diethylaminoethyl-6-aminoindazoles and 60 ml of 10% sulfuric acid was heated in a sealed tube at 160-180° for 20 hours. At the end of the reaction, the dark-brown solution was cooled and made alkaline with concentrated sodium hydroxide solution and the alkaline solution extracted with ether. The ether extract was dried and evaporated. We obtained 1.62 g of

1-diethylaminoethyl-6-aminoindazole, whose picrate had m.p. 161-162°. The alkaline solution was acidified to congo with 20% sulfuric acid, then ammonia added to a weakly alkaline reaction and the liberated oil extracted with ether. We obtained 3.04 g of a colorless substance, which had m.p. 90-91° (2.45 g) after recrystallization from 20 ml of benzene and drying in vacuum. The yield was 35%. 6-Hydroxy-2-diethylaminoethylindazole formed colorless prisms with m.p. 90-91°, which were readily soluble in alcohol, ether, benzene, acetone, alkali and acid and more difficultly so in water.

Found %: C 66.91; H 8.21; N 18.12. $C_{13}H_{19}ON_3$. Calculated %: C 66.92; H 8.21; N 18.01.

3-Chloro-6-nitro-2-diethylaminoethylindazole. Into a solution of 1.5 g of the hydrochloride of 6-nitro-2-diethylaminoethylindazole in 10 ml of water, stirred at 45-50°, was slowly passed chlorine obtained from 0.39 g of potassium permanganate and 6 ml of conc. HCl. When the chlorine had been passed in, stirring was continued for a further half an hour. The reaction mixture was then made alkaline to phenolphthalein with 2 N sodium hydroxide solution with cooling. The yellow precipitate was collected, washed with water and dried. We obtained 1.37 g (92%) of a substance with m.p. 75-80°. After two recrystallizations from n-heptane, the yellow prisms had m.p. 83-84° and were readily soluble in alcohol, acetone, benzene, dichloroethane and ether, more difficultly so in petroleum ether and insoluble in water.

Found %: N 18.83; Cl 11.66. $C_{13}H_{17}O_2N_4Cl$. Calculated %: N 18.88; Cl 11.95.

3-Chloro-6-nitro-2-dimethylaminoethylindazole was obtained similarly in 91% yield. It appeared as yellow prisms [from a mixture of benzene and n-heptane (1:1)] with m.p. 116.5-117°, which were readily soluble in acetone, alcohol, dichloroethane and ether, more difficultly so in petroleum ether and insoluble in water.

Found %: N 20.95; Cl 13.07. $C_{11}H_{13}O_2N_4Cl$. Calculated %: N 20.85; Cl 13.20.

β-[2-(6-Nitroindazole)-ethyl]-diethylmethylammonium iodide. a) 3 g of methyl iodide was added to a solution of 1.32 g of 6-nitro-2-diethylaminoethylindazole in 10 ml of anhydrous benzene. The mixture was left overnight. The precipitate was collected and washed with anhydrous benzene. We obtained 1.92 g (95%) of substance; the narrow, yellow plates with m.p. 177-178° (with decomp.) were readily soluble in water, more difficultly so in alcohol and acetone and insoluble in ether. For analysis, the substance was recrystallized from anhydrous alcohol, when the melting point did not change.

Found %: C 41.64; H 5.19; N 13.57; I 31.21. $C_{14}H_{21}O_2N_4I$. Calculated %: C 41.70; H 5.24; N 13.86; I 31.39.

b) A mixture of 1.32 g of 6-nitro-2-diethylaminoethylindazole and 3 ml of methyl iodide was heated in a sealed tube at 100° for six hours. At the end of the reaction, the precipitate was collected and washed with dry benzene; we obtained 2.01 g of a light-yellow compound with m.p. 177-178° (with decomp.), whose melting point was not changed after recrystallization. A mixed melting point with the compound obtained in experiment "a" was not depressed. The yield was quantitative.

β-[1-(6-Nitroindazole)-ethyl]-trimethylammonium iodide was obtained by the above method in 96.2% yield. After recrystallization from aqueous alcohol, the substance appeared as yellow platelets with m.p. 257 to 258° (with decomp.), which were soluble in water, more difficultly so in alcohol and acetone and insoluble in benzene and ether.

Found %: C 38.57; H 4.33; N 14.94; I 33.88. $C_{12}H_{17}O_2N_4I$. Calculated %: C 38.31; H 4.55; N 14.89; I 33.73.

SUMMARY

1. The 1- and 2-diethylaminoethyl and -dimethylaminoethyl derivatives of 6-nitroindazole, 6-aminoindazole and 3-chloro-6-nitroindazole, 1- and 2-dimethylaminoethylindazoles, 1- and 2-dimethylaminoethyl-3-chlorindazoles and 2-diethylaminoethyl-6-hydroxyindazole were prepared. The mixtures of 1- and 2-isomers obtained were resolved by fractional crystallization of the hydrochlorides or fractional precipitation of the picrates. The structures of the 1- and 2-substituted indazoles obtained were proved by comparison of their ultraviolet spectra with the spectra of the corresponding 1- and 2-methylindazoles.

2. It was shown that when a mixture of 1- and 2-diethylaminoethyl-6-aminoindazoles was heated with 10% sulfuric acid, only the 2-substituted derivative was converted into the 6-hydroxy derivative, while in the 1-substituted derivative, the amino group in position 6 was not replaced by hydroxyl.

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REACTION OF PHENAZINE AND PHENAZINE N-OXIDE WITH ORGANOMAGNESIUM HALIDES

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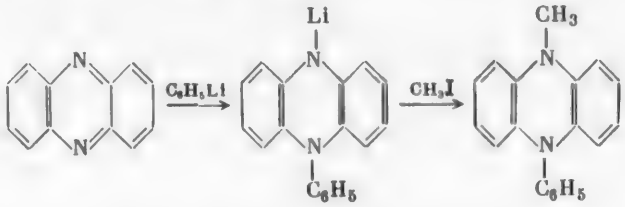
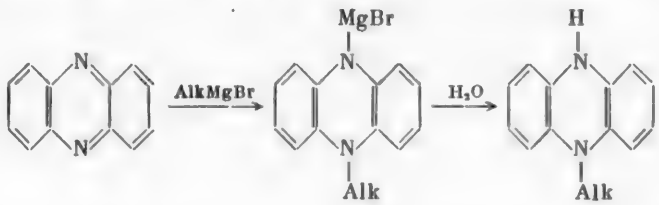
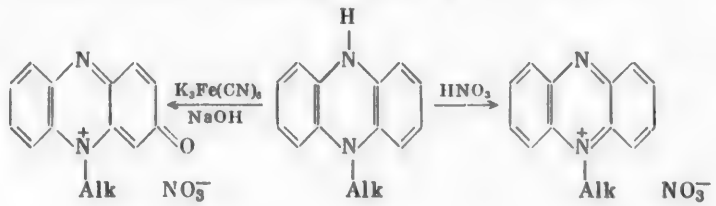
The reaction of phenazine with organomagnesium halides has not been studied up to now. There is information in the literature on the action of organomagnesium halides on quaternary salts of phenazine. Freund and Richard [1] found that the action of alkylmagnesium halides on flavinduline formed phenylalkyldihydrophenazines, whose structure they were unable to establish exactly. Later, McIlwain [2] and Hilleman [3] investigated the reaction of salts of N-methylphenazine with methylmagnesium iodide and showed that this yielded a certain amount of 9,10-dimethyldihydrophenazine. In 1950, Mikhailov and Blokhina added phenyllithium to phenazine. Without being isolated, the 9-lithium-10-phenyldihydrophenazine formed was converted into 9-methyl-10-phenyldihydrophenazine by the action of methyl iodide.



We established that alkylmagnesium bromides react with phenazine similarly to phenyllithium. Decomposition of the addition product with water yields 9-alkyl-9,10-dihydrophenazines.



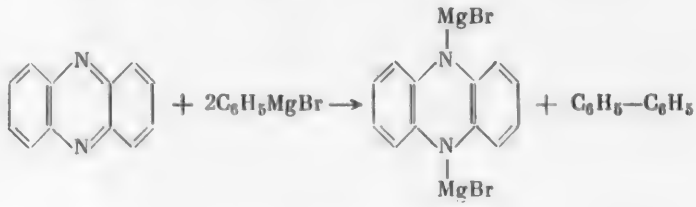
We did not isolate these dihydro derivatives, which are unstable in air. We oxidized them with dilute nitric acid into the corresponding quaternary salts of phenazine (in yields of about 39%) or oxidized them in alkaline solution with potassium ferricyanide into 9-alkylphenazinones-2 (yields of up to 50%).



Our experiments showed that in order to obtain the given yields, it was necessary to take not less than 2.5 moles of Grignard reagent per mole of phenazine.

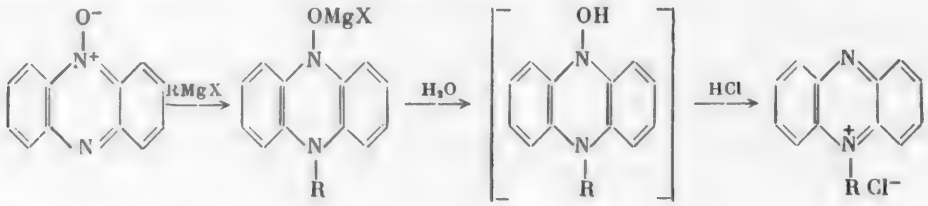
The action of alkylmagnesium halides on phenazine and its derivatives is of interest for the preparation of quaternary salts of phenazine with certain higher alkyls at the nitrogen atom. Up to now it was not possible to prepare salts of N-isopropyl- and N-cyclohexylphenazine.* By means of isopropylmagnesium bromide and cyclohexylmagnesium bromide, we prepared these quaternary salts of phenazine in yields of 37 and 35%, respectively.

The reaction of phenylmagnesium bromide with phenazine proceeded differently from that with alkylmagnesium bromides. If the reaction product of phenazine and phenylmagnesium bromide was treated with water, it formed a blue precipitate of phenazhydrin, a molecular compound of dihydrophenazine and unreacted phenazine. Mikhailov and Blokhina [4] observed a similar phenomenon when phenazine was treated with phenyllithium at an elevated temperature. Simultaneously, these authors isolated diphenyl from the reaction products. We also detected diphenyl. Since dihydrophenazine may only be formed from the dimagnesium derivative, the reaction may be represented by the following over-all equation



We did not investigate the mechanism of this reaction.

The reaction of organomagnesium halides with phenazine N-oxide was of considerably greater interest from the preparative point of view. As would be expected, the Grignard reaction added to the oxide molecule. Treatment of the reaction product with mineral acid yielded a quaternary salt.

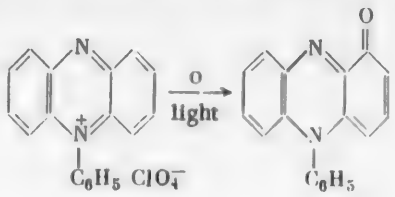


The difficulty of reacting organomagnesium halides with phenazine and phenazine oxide was caused by the low solubility of phenazine and its oxide in ether. We were obliged to mix a suspension of the reagents with an ether solution of the Grignard reagent on a shaker in the presence of glass beads for a long time. In the case of both phenazine and its oxide, a large excess of organomagnesium halide was required.

The reaction of phenazine oxide with arylmagnesium halides was of particular interest since it gave N-arylphenazonium salts, which could not be obtained from phenazine by other methods up to now. We synthesized two such salts, N-phenylphenazonium perchlorate and N-p-tolylphenazonium perchlorate. The ultraviolet absorption curves of N-phenylphenazonium and N-ethylphenazonium perchlorates were very similar, but the maxima of the phenyl derivative (λ_{1max} 386 mμ, ϵ_1 $2.24 \cdot 10^4$, λ_{2max} 260 mμ, ϵ_2 $6.60 \cdot 10^4$) were not shifted toward longer wavelengths as might be expected, but toward shorter wavelengths in comparison with the maxima of the N-ethyl derivative (λ_{1max} 390 mμ, ϵ_1 $2.12 \cdot 10^4$, λ_{2max} 261 mμ, ϵ_2 $5.80 \cdot 10^4$). This and also the fact that, in contrast to the N-ethyl derivative, the N-phenyl derivative did not fluoresce under an ultraviolet lamp supports the hypothesis that, under the effect of steric hindrance, the phenyl group in the N-phenylphenazonium cation is forced out of the plane of the phenazine nucleus.

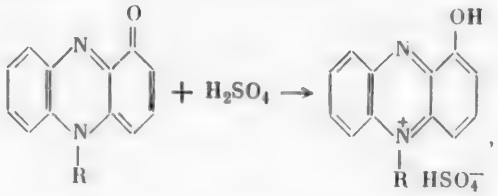
*Esters of o-nitrobenzenesulfonic acid are most convenient for the preparation of quaternary salts of phenazine [5], but the isopropyl and cyclohexyl esters of this acid are unstable compounds.

In aqueous solution, N-phenylphenazonium perchlorate is very readily oxidized in the light. This yielded the previously unknown phenyl analog of the natural antibiotic pyocyanin – 10-phenylphenazinone-1.



An alcohol solution of 10-phenylphenazinone-1 had a green color and, like an alcohol solution of 10-ethylphenazinone-1, a broad maximum between 720 and 760 mμ.

The absorption curves of the two phenazinones in benzene clearly showed two absorption maxima, at 695 mμ (more intense) and 750 mμ for N-phenylphenazinone and at 685 mμ (more intense) and 740 mμ for N-ethylphenazinone. When acidified with sulfuric acid, the blue alcohol solutions of phenazinones became red as a result of the formation of phenazinol salts



which have absorption maxima at 542 mμ with R = C_2H_5 and at 555 mμ with R = C_6H_5.

Decker and Pschorr [6] showed that the action of benzylmagnesium chloride on N-methylquinolone and on N-methylisoquinolone, with subsequent decomposition of the reaction products with acid yielded the chloromethylates of 2-benzylquinoline and 1-benzylisoquinoline. Since there is a known analogy in structure and properties between N-alkylquinolones and N-alkylphenazinones, we attempted to add ethylmagnesium bromide to 9-ethylphenazinone-2 and to 10-ethylphenazinone-1. However, the reactions did not occur even when the components were boiled for a long time in di-n-butyl ether. The starting materials were recovered almost completely.

EXPERIMENTAL

N-Ethylphenazinium perchlorate. 5.4 g (0.03 mole) of phenazine and 100 ml of dry ether were shaken with glass beads on an electric shaker for one hour. Then, when the phenazine had been powdered sufficiently, with continued shaking five 7.5-ml portions of a 2 N ether solution of ethylmagnesium bromide were added at one-hour intervals, making a total of 37.5 ml (0.075 mole). When the last portion had been added, the reaction mixture was shaken for a further six hours. On the following day, it was decomposed with 60 ml of a saturated ammonium chloride solution. The light-brown ether layer was separated from the colorless aqueous layer and the latter was extracted with a small amount of ether. The combined ether extracts were dried with sodium sulfate and a stream of dry hydrogen chloride passed through the ether for one hour. A precipitate formed which gradually turned green in air. It was collected and the residual ether evaporated almost to dryness. The green precipitate was combined with the previous one and the two suspended in 50 ml of 25% nitric acid. The mixture was heated to boiling then cooled, the solution decanted and the residual brown tar extracted three times with 80-ml portions of boiling water. The combined aqueous extracts were neutralized with sodium carbonate and the precipitated phenazine (1.2 g, m.p. 172°) collected. The filtrate was acidified, boiled with a small amount of activated charcoal and evaporated to small volume. Sodium perchlorate was added to the solution. Ethylphenazine perchlorate precipitated in a yield of 2.65 g (39%). After recrystallization from water, the yellow prisms had m.p. 245° (with decomp., uncorr.).

Found %: Cl 11.40, 11.60. $C_{14}H_{13}O_4N_2Cl$. Calculated %: Cl 11.54.

If 1 mole of ethylmagnesium bromide was used per mole of phenazine, the yield of ethylphenazine per-

chlorate fell to 19.5%; with 2 moles of ethylmagnesium bromide, the yield was 32.5%. The use of more than 2.5 moles of ethylmagnesium bromide per mole of phenazine did not increase the yield.

9-Ethylphenazinone-2. 5.4 g (0.03 mole) of phenazine was treated with 37.5 ml of 2 N ethylmagnesium bromide solution (0.075 mole) in dry ether as above. After decomposition of the reaction mixture with ammonium chloride solution, the ether layer was separated, washed with water and placed in a three-necked flask fitted with a stirrer, a reflux condenser and a dropping funnel. To the ether solution was added a solution of 40 g of potassium ferricyanide in 300 ml of water and then, with vigorous stirring, a solution of 5 g of sodium hydroxide in 50 ml of water was added dropwise over a period of two hours. The color of the emulsion changed from yellow to red. The mixture was stirred for a further six hours and then the ether layer separated and evaporated to dryness. The aqueous layer was extracted several times with chloroform, the extract concentrated to small volume and then, after dissolving the residue from the ether solution in it, it was chromatographed on aluminum oxide. We isolated 2.9 g (43%) of 9-ethylphenazinone-2 with m.p. 174° and 1 g of phenazine with m.p. 172°.

9-n-Propylphenazinone-2. 5.4 g (0.03 mole) of phenazine in 100 ml of dry ether was treated with 40 ml of 1.9 N propylmagnesium bromide solution as above. After decomposition of the reaction mixture with 70 ml of a saturated solution of ammonium chloride, the dihydro compound was oxidized in an aqueous emulsion as described above. As a result of chromatography, we isolated 2.7 g (38%) of 9-n-propylphenazinone which, after recrystallization from water, had m.p. 166-168° and did not depress the melting point of an authentic preparation.

N-Isopropylphenazinium perchlorate was prepared from 5.4 g of phenazine in 100 ml of ether and 45 ml of a 1.7 N ether solution of isopropylmagnesium bromide. The yield was 3.6 g (37%) and after recrystallization from water, the substance had m.p. 196-197° (with decomp.).

Found %: Cl 10.80. $C_{15}H_{15}O_4N_2Cl$. Calculated %: Cl 10.99.

9-n-Butylphenazinone-2 was obtained from the appropriate starting materials in a yield of 3 g (43%). After recrystallization from water, the substance had m.p. 196-198° (uncorr.). A mixed melting point with an authentic preparation was not depressed.

N-Cyclohexylphenazinium perchlorate was synthesized from 5.4 g of phenazine in 100 ml of ether and 38 ml of a 2 N ether solution of cyclohexylmagnesium bromide in a yield of 3.7 g (35%). After recrystallization from water, the orange prisms had m.p. 169-171° (with decomp.).

Found %: Cl 9.60, 9.42. $C_{18}H_{19}O_4N_2Cl$. Calculated %: Cl 9.78.

9-Cyclohexylphenazinone-2 was obtained from the same starting materials in a yield of 3.3 g (40%). After recrystallization from aqueous methanol, the substance formed red tablets with m.p. 146-150° and with an absorption maxima in alcohol solution at 363 and 522 mμ.

Found %: N 9.90, 10.02. $C_{18}H_{18}ON_2$. Calculated %: N 10.05.

9-Cyclohexylphenazinone-2 gave a salt with hydrochloric acid, which was recrystallized from 5% hydrochloric acid, but did not have a sharp melting point. The absorption maxima of the salt in 5% hydrochloric acid were at 259 and 392 mμ.

Found %: Cl 10.90, 10.94. $C_{18}H_{19}ON_2Cl$. Calculated %: Cl 11.10.

10-Cyclohexylphenazinone-1. A solution of 3.62 g (0.01 mole) of N-cyclohexylphenazinium perchlorate and 2 g of sodium carbonate in 1 liter of water was left in sunlight for three days. Then, after a further addition of sodium carbonate, the dark-blue solution formed was extracted with chloroform. The chloroform extract was chromatographed on aluminum oxide. We obtained 1.36 g (50%) of blue needles of phenazinone with m.p. 148-149°. The absorption maximum of an alcohol solution was not sharp and lay at about 750 mμ; phenazinone was readily soluble in chloroform and difficultly so in water.

Found %: N 9.94, 10.03. $C_{18}H_{18}ON_2$. Calculated %: N 10.05.

Reaction of phenazine with phenylmagnesium bromide. 5.4 g of phenazine in 100 ml of dry ether was placed in a bottle with a ground-glass stopper, containing glass beads. 16 ml of 2 N phenylmagnesium bromide solution was added to the mixture, cooled in ice water. The mixture was shaken mechanically for 12 hours. Decomposition of the reaction product with ammonium chloride solution produced a dark-blue precipitate, which was collected, washed several times with ammonium chloride solution and with water, and dried in a desiccator

over sulfuric acid. The dark-blue powder obtained (5 g) was found to be phenazhydrin, since after recrystallization from alcohol, it formed blue needles with m.p. 209°, which did not depress the melting point of phenazhydrin, obtained by another method. When boiled with dilute nitric acid, it was converted into phenazine with m.p. 171°. By means of chromatography on aluminum oxide, the ether solution yielded diphenyl with m.p. 67-68°. Performing the reaction in benzene gave the same result. If insufficient phenylmagnesium bromide were used, less phenazhydrin was isolated and phenazine remained in the ether; with excess phenylmagnesium bromide, phenazhydrin was not precipitated immediately after decomposition of the reaction mixture with ammonium chloride solution. All attempts to prepare aposafranone (9-phenylphenazinone-2) by oxidation of the ether extract with potassium ferricyanide were unsuccessful.

N-Ethylphenazinium perchlorate from phenazine N-oxide and ethylmagnesium bromide. 3.92 g (0.02 mole) of phenazine N-oxide in 80 ml of dry ether was treated with 30 ml of a 2.1 N ether solution of ethylmagnesium bromide in the same way as described above in the reaction of ethylmagnesium bromide with phenazine. The mixture was decomposed with 30 g of ice and 50 ml of 20% hydrochloric acid. The aqueous layer was separated, neutralized to a just weakly acid reaction with sodium carbonate, filtered free from precipitate and evaporated to small volume. The quaternary salt was precipitated with sodium perchlorate. The yield was 2.20 g (34%) and after recrystallization from water, the substance had m.p. 245° (uncorr.). Decreasing the amount of ethylmagnesium bromide sharply reduced the yield while increasing it above 3 moles per mole of phenazine oxide did not give an increase in yield.

N-phenylphenazinium perchlorate was obtained as above from 5.88 g of phenazine N-oxide in 120 ml of dry ether and 8 ml of a 1.7 N ether solution of phenylmagnesium bromide. The yield was 3.6 g (32%) and, after recrystallization from 30% alcohol, the brown prisms had m.p. 262°.

10-Phenylphenazinone-1. A solution of 3.72 g (0.01 mole) of N-phenylphenazinium perchlorate and 1 g of sodium carbonate in 500 ml of water was irradiated with a high-pressure mercury lamp for ten hours. The color of the solution changed from yellow to blue-violet. More sodium carbonate was added to the solution, which was extracted with chloroform. After removal of part of the chloroform, the residue was chromatographed on aluminum oxide. We obtained 1.5 g (55%) of blue needles. After recrystallization from 50% alcohol, the substance had m.p. 224-225° (uncorr.).

Found %: N 10.08, 9.99. $C_{18}H_{12}ON_2$. Calculated %: N 10.28.

N-p-Tolylphenazinium perchlorate was obtained similarly to the other quaternary salts from 3.92 g (0.02 mole) of phenazine N-oxide in 80 ml of ether and 60 ml of a 1 N solution of p-tolylmagnesium bromide. The yield was 3.1 g (37.5%) and, after recrystallization from 50% alcohol, the brown cubes had m.p. 255-256°.

Found %: N 9.32, 9.48. $C_{19}H_{15}O_4N_2Cl$. Calculated %: N 9.60.

SUMMARY

The action of organomagnesium halide compounds on phenazine yielded 9-alkyl-9,10-dihydrophenazines, which gave quaternary salts of phenazine, when oxidized in an acid medium. Quaternary salts of phenazine were also synthesized by the action of organomagnesium halides on phenazine oxide and decomposition of the reaction products with acid. N-Phenylphenazinium perchlorate was prepared by the latter method and oxidized photochemically to 9-phenylphenazinone-2.

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SYNTHESES IN THE FIELD OF CHROMONECARBOXYLIC-2 ACID DERIVATIVES

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It is known that certain derivatives of chromone are physiologically active materials. Thus, for example, kellin (2-methyl-5,8-dimethoxy-6,7-furanochromone) has come into use as a spasmolytic. Properties similar to those of kellin are shown by other, simpler-substituted chromones [1-4], including chromonecarboxylic-2 acid and its esters. It was recently found that chromonecarboxylic-2 acid possesses a clearly expressed anticonvulsive action [5].

In order to find new pharmacologically active substances and to elucidate the problem of the relation between activity and structure in the chromone series, we synthesized certain new derivatives of chromonecarboxylic-2 acid. While there is data available in the literature on various aliphatic esters of chromonecarboxylic-2 acid, obtained by esterification (for example, [1, 3]), of the aryl esters the only one known is the phenyl, which was formed in low yield (18%) by the reaction chromonecarboxylic-2 acid with phenol in the presence of sulfuric acid [3]. In this work we synthesized aryl esters of chromonecarboxylic-2 acid (I-VIII, see table), starting from the acid chloride and appropriate phenols. In most cases, the acid chloride was used as a pyridine solution, obtained by treating a suspension of chromonecarboxylic-2 acid in pyridine with thionyl chloride.

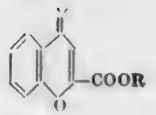
The preparation of the acid chloride of chromonecarboxylic-2 acid in the free state was of interest in itself, since up to now there has been no information on the existence of acid chlorides of γ-pyrone- and γ-benzopyronecarboxylic-2 acids. An attempt to convert chromonecarboxylic-2 acid into its acid chloride by the action of thionyl chloride, described previously, was unsuccessful [3]. The substance isolated contained more chlorine than the amount calculated for the acid chloride. A detailed investigation of this reaction, which we undertook, showed that when chromonecarboxylic-2 acid was boiled (four hours) with a large excess of thionyl chloride, together with the corresponding acid chloride, a considerable amount of a chlorine-containing substance of unknown structure was formed, which had m.p. 93-94° and whose yield increased with an increase in the heating time. This substance was also obtained by boiling a solution of the acid chloride in thionyl chloride. We are determining its structure at the present time.

To obtain a high yield (88%) of the acid chloride by the reaction of chromonecarboxylic-2 acid and excess thionyl chloride, it was necessary to perform the reaction in a solvent, for example, dichloroethane or dioxane.

We developed a convenient procedure for synthesizing chromonecarboxylic-2 acid on a large laboratory scale. Chromonecarboxylic-2 acid can be obtained by cyclization of the difficultly accessible phenoxyfumaric acid in the presence of sulfuric acid or sulfuric acid and acetyl chloride [6]. Another, less difficult method consists of the condensation of o-hydroxyacetophenone with diethyl oxalate under the action of alkaline agents (sodium [7], sodium hydride [1] or sodium ethylate [3]) into the sodio derivative of ethyl o-hydroxybenzoylpyruvate cyclization of this under the action of mineral acid into ethyl chromonecarboxylate-2 and hydrolysis of the latter.

o-Hydroxyacetophenone was used as the starting material for the synthesis. Many papers [8-13] have been devoted to the problem of synthesizing this compound from phenyl acetate by the Fries rearrangement. Nonetheless, up to now no rapid and economical laboratory method has been put forward for preparing o-hydroxyacetophenone in large amounts. We should note that certain communications on the predominant migration of the acetyl group into the ortho position should be treated with care. In a repeat of the work in [14] by a known method

Aryl Esters of Chromonecarboxylic Acid



Substance No.	R	Empirical formula	Yield (%)	Melting point	Found (%)		Calc. (%)	
					C	H	C	H
(I)	C_6H_5		86.5	109.5—110° *	—	—	—	—
(II)	2-$CH_3OC_6H_4$	$C_{17}H_{12}O_5$	77.7	130.5—131 **	68.98	4.17	68.92	4.08
(III)	3-$CH_3OC_6H_4$	$C_{17}H_{12}O_5$	79.3	124.5—125.2	68.95	4.25	68.92	4.08
(IV)	4-$CH_3OC_6H_4$	$C_{17}H_{12}O_5$	69.2	115 —115.5	69.32	4.34	68.92	4.08
(V)	3,5-$(CH_3O)_2C_6H_3$	$C_{18}H_{14}O_6$	82.8	134.8—135.5	66.35	4.29	66.26	4.32
(VI)	2-$OHCC_6H_4$	$C_{16}H_{10}O_6$	85.0	147.5—148	69.66	3.61	69.39	3.43
(VII)	α-Naphthyl	$C_{20}H_{12}O_4$	77.8	132 —133	75.65	3.64	75.94	3.82
(VIII)	β-Naphthyl	$C_{20}H_{12}O_4$	70.2	156 —156.5	76.11	3.93	75.94	3.82

*According to data in [3]: m.p. 104-105°.

**Esters (II-VIII) were recrystallized from alcohol.

[10], o-hydroxyacetophenone was isolated in 25% yield instead of 70%. In exactly the same way, we were unable to reproduce experiments from [15], according to which phenyl acetate is converted into o-hydroxyacetophenone in 70-80% yield under the action of not only 1 mole, but also 0.25 mole of aluminum chloride. Phenyl acetate could be rearranged in amounts of up to 5 moles (larger amounts were not tried) considerably more simply and rapidly if the whole of the ester was added directly to the aluminum chloride with vigorous stirring. The yield of o-hydroxyacetophenone was 38-39% (together with 50-53% of the para-isomer).

We used sodium ethylate as the condensing agent in the reaction of o-hydroxyacetophenone with diethyl oxalate [3]. The condensation was carried out by adding a mixture of o-hydroxyacetophenone (2 moles) and diethyl oxalate to a solution of sodium ethylate in alcohol with subsequent heating of the reaction mixture. The sodio derivative of ethyl o-hydroxybenzoylpyruvate formed was converted into chromonecarboxylic-2 acid by boiling first with concentrated and then with dilute hydrochloric acid. The yield of pure acid was 72-80%.

In order to determine the effect of introducing a methoxy group into the benzene nucleus of ethyl chromonecarboxylate-2 on the change in the anticonvulsive activity, we synthesized the ethyl esters of 6- and 7-methoxychromonecarboxylic-2 acids.

The results of the pharmacological tests on some of the preparations obtained will be reported separately.

EXPERIMENTAL

Preparation of o-hydroxyacetophenone. 1 kg of anhydrous aluminum chloride was placed in a round-bottomed flask (5 liter), fitted with a mechanical stirrer, capable of moving the precipitate from the bottom. The flask was set in an oil bath. Over a period of 1-3 minutes, 680.5 g of phenyl acetate was added to the aluminum chloride and the stirrer started. The reaction mixture heated up (120-130°) and a vigorous evolution of hydrogen chloride occurred. Stirring was continued until the contents of the flask thickened (~30 minutes). The oil bath was rapidly heated to 130-140° and kept at this temperature for two hours. The cooled melt was decomposed with ice and water in such a way that the mixture did not boil. The o-hydroxyacetophenone was distilled from the same flask with superheated steam (150-180°) and extracted from the distillate with carbon tetrachloride with salting out. The combined extracts were dried with sodium sulfate. The solvent was evaporated. Vacuum distillation yielded 259-264 g (38-39%) of o-hydroxyacetophenone with b.p. 104-106° (20 mm) and $n^{20}D$ 1.5588. The pure substance had b.p. 106° (20 mm), $n^{20}D$ 1.5593. Literature data: b.p. 100° (14 mm) [16], 105-106° (20 mm) [8], $n^{20}D$ 1.5593 [16]. p-Hydroxyacetophenone crystallized in the distillation flask on cooling; the yield of impure material was 340-362 g (50-53%).

Preparation of chromonecarboxylic-2 acid. In a round-bottomed flask (5 liter), fitted with a three-necked adaptor, a reflux condenser and a mechanical stirrer, was prepared a solution of sodium ethylate (46 g of sodium and 1 liter of anhydrous alcohol). The solution was cooled to 30-40° and a mixture of 272.2 g of o-hydroxyacetophenone and 438.3 g of diethyl oxalate was added to it rapidly (1-3 minutes with stirring) through one neck of the adaptor. The reaction mixture was heated (60-70°) for three hours. A yellow precipitate of the sodio derivative

of ethyl o-hydroxybenzoylpyruvate separated. The mixture was cooled to 20-30°, 280 ml of conc. HCl added and the mixture boiled for 30 minutes. Then, without cooling, a solution of 920 ml of conc. HCl in 1.4 liters of water was added to the contents of the flask, which were boiled for a further three hours. The chromonecarboxylic-2 acid liberated was collected on the following day, recrystallized from 70% alcohol (~3.5 liters) with decolorization with activated charcoal (30-60 g). We obtained a first fraction of chromonecarboxylic-2 acid, weighing 227-247 g (dried at 105°). A further 48-57 g of chromonecarboxylic-2 acid was isolated from the mother solution. The total yield was 275-304 g (72-80%) and the m.p. 250-251° (with decomp.). Literature data [7]: m.p. 252° (with decomp.).

The Na-salt was isolated as colorless flakes by the addition of alcohol to a concentrated solution, prepared by treating a slight excess of chromonecarboxylic-2 acid with sodium bicarbonate in water.

Found %: C 56.48; H 2.55. $C_{10}H_5O_4Na$. Calculated %: C 56.61; H 2.37.

Reaction of chromonecarboxylic-2 acid with thionyl chloride. a) 38 g of chromonecarboxylic-2 acid, 57 ml of $SOCl_2$ and 90 ml of dichloroethane were boiled until all the acid dissolved (7-8 hours) and then heated for a further 30 minutes. The dichloroethane and $SOCl_2$ were removed in vacuum and the residue treated with 60 ml of petroleum ether, filtered off, washed with petroleum ether (2 x 30 ml) and dried. The yield of the light-yellow chromonecarboxylyl-2 chloride with m.p. 103-105° was 36.7 g (88%). When recrystallized from petroleum ether, the substance had m.p. 105.5-106.5°. It formed short, colorless needles.

Found %: C 57.80; H 2.59; Cl 17.04. $C_{10}H_5O_3Cl$. Calculated %: C 57.57; H 2.42; Cl 17.00.

The anilide (from the acid chloride and excess aniline in dichloroethane with cooling) had m.p. 225-225.5°.

Found %: N 5.29. $C_{16}H_{11}O_3N$. Calculated %: N 5.28.

When shaken with an aqueous solution of sodium bicarbonate, the petroleum ether solutions yielded 2 g of a chlorine-containing substance with m.p. 93-94°.

b) Chromonecarboxylic-2 acid (38 g) was heated with $SOCl_2$ (100 ml) for nine hours (the excess thionyl chloride was removed at normal pressure and the residue treated with aqueous bicarbonate in the absence of solvent); the yield of the substance with m.p. 93-94° was 31.3 g (4.2 g of chromonecarboxylic acid was recovered).

Preparation of aryl esters of chromonecarboxylic-2 acid. Phenyl ester (I). With cooling, 1.4 g of $SOCl_2$ was added to 1.9 g of chromonecarboxylic-2 acid in 7 ml of anhydrous pyridine, the precipitate ground until it dissolved (~5 minutes) and then a solution of 1.1 g of phenol in 5 ml of absolute ether added. After 45 minutes (without cooling, but with periodic stirring), 15 ml of benzene was added and the mixture poured into 10 ml of conc. HCl with ice. The precipitate was extracted with benzene (in the case of esters V and VI-VIII benzene was not added and the precipitate was filtered off and washed with ether) and the extracts washed with sodium bicarbonate solution and water and dried with sodium sulfate. The benzene was removed in vacuum and the residue treated with a mixture of ether and petroleum ether. We obtained 2.3 g of the phenyl ester of chromonecarboxylic-2 acid with m.p. 108.5-109.5°. It was purified by recrystallization from petroleum ether (activated charcoal).

o-Formylphenyl ester (VI). A solution of 1.46 g of salicylaldehyde in 3 ml of pyridine was added to 2.1 g of chromonecarboxylyl-2 chloride in 7 ml of pyridine at 0°. After one hour (20°), 20 ml of benzene was added and the mixture poured into 15 ml of conc. HCl and ice. The precipitate was collected, washed with dilute hydrochloric acid, sodium bicarbonate and water and dried. We obtained 2.5 g of ester (VI) with m.p. 146-147°.

Ethyl ester of 7-methoxychromonecarboxylic-2 acid. 16.6 g of 2-hydroxy-4-methoxyacetophenone was condensed with 29.2 g of diethyloxalate in the presence of sodium ethylate (2.3 g of Na and 50 ml of anhydrous alcohol) as in the preparation of chromonecarboxylic-2 acid. Then 14 ml of conc. HCl was added, the mixture boiled for 30 minutes and cooled and 0.5 liter of water added. The precipitate was collected, dried (weight 20 g) and treated with aqueous sodium bicarbonate to give the ethyl ester of 7-methoxychromonecarboxylic-2 acid; the yield was 16 g (64.5%). The m.p. was 122-123° (from alcohol and benzene).

Found %: C 62.91; H 4.81. $C_{13}H_{12}O_5$. Calculated %: C 62.89; H 4.87.

Acidification of the bicarbonate solution precipitated 2.7 g of 7-methoxychromonecarboxylic-2 acid. The m.p. was 265° (with decomp.; rapid heating). According to data [17]: m.p. 261° (with decomp.).

Ethyl ester of 6-methoxychromonecarboxylic-2 acid. This was synthesized similarly to the ethyl ester of chromonecarboxylic-2 acid [3], starting from 2-hydroxy-5-methoxyacetophenone. The m.p. was 100.5-101* (from 50% alcohol and ligroin).

Found %: C 63.08; H 4.92. $C_{13}H_{12}O_5$. Calculated %: C 62.89; H 4.87.

SUMMARY

1. A series of aryl esters of chromonecarboxylic-2 acid was synthesized.

2. A study was made of the reaction of thionyl chloride with chromonecarboxylic-2 acid and the optimal conditions for preparing the acid chloride of the latter found.

3. A simplified method is presented for preparing chromonecarboxylic-2 acid on a large laboratory scale.

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CYANINE DYES FROM SEVEN-MEMBERED HETEROCYCLIC SYSTEMS

I. STYRYLS OF THE DIHYDROBENZOHEPTA-1,5-THIAZINE SERIES

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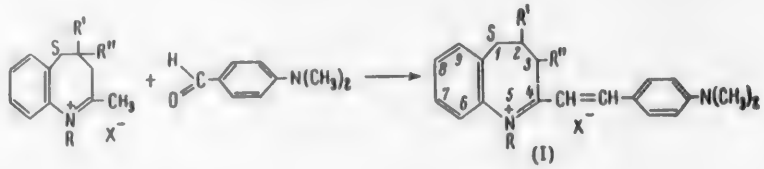
We previously showed [1] that the bromomethylate and bromoethylate of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine condensed readily with p-dimethylaminobenzaldehyde with the formation of dyes, styryls. In subsequent communications [2] it was noted that other quaternary salts of the dihydrobenzohepta-1,5-thiazine series we synthesized had an active methyl group in position 4.

In the present communication we describe the synthesis of p-dimethylaminostyryls from seven-membered heterocyclic systems of the general formula (I) and some of their optical properties were investigated. The styryls were very readily obtained from the quaternary salts of dihydrobenzohepta-1,5-thiazine derivatives. For this purpose it was sufficient to heat equimolecular amounts of the quaternary salt and p-dimethylaminobenzaldehyde in acetic anhydride on a water bath for several minutes.



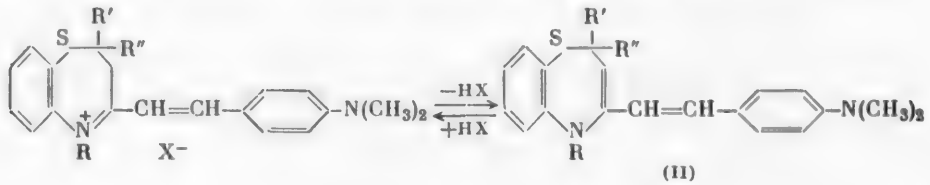
(I)

The properties of the styryls of general formula (I) are presented in the table.

As the data presented in the table show, the replacement of the hydrogen atoms in position 2 by methyl radicals does not affect the color of the styryls. Replacement of the alkyl groups in position 5 by phenyl shifts the absorption maximum into the long-wave region of the spectrum by 20-25 mμ.

It is interesting to note that replacement of the sulfur atom in the seven-membered ring by an NH group has no effect at all on the color of the styryls. Thus, for example, the nitrogen analog of dye No. 8, obtained by us previously [3] from the bromophenylate of 2,2,4-trimethyldihydrobenzohepta-1,5-diazine, also has an absorption maximum at 545 mμ.

The action of alkali on alcohol solutions of the styryls produces decolorization. The styryl bases obtained in this way, which apparently have structure (II), again form the original dyes with mineral acids.

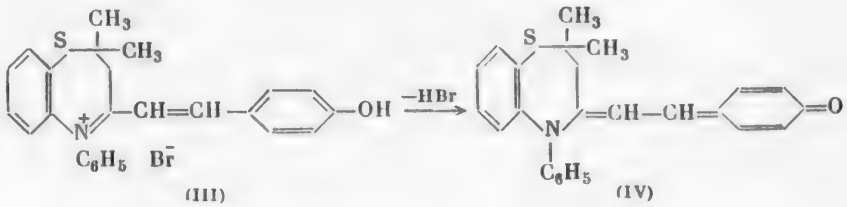


(II)

In the last column of the table are presented the absorption maxima of alcohol solutions of the free bases of general formula (II) for dyes 6-8.

Dye No.	R′	R″	R	X	λ_{max} in ethanol (mμ)	M.p.	Yield (%)	λ_{max} of styryl bases (mμ)
1	H	H	C_2H_5	ClO_4	520	211°	68	—
2	H	H	C_6H_5	ClO_4	546	228	85	—
3	H	CH_3	CH_3	I	522	230	51	—
4	H	CH_3	C_2H_5	ClO_4	520	230	72	—
5	H	CH_3	C_6H_5	I	545	232	46	—
6	CH_3	CH_3	CH_3	Br	522	230	56	400
7	CH_3	CH_3	C_2H_5	Br	523	247	51	405
8	CH_3	CH_3	C_6H_5	Br	547	210	93	410

The condensation of the bromophenylate of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine with p-hydroxybenzaldehyde formed the hydroxystyryl of structure (III).



(III) (IV)

The action of ammonia produced elimination of acid due to the hydrogen of the hydroxyl group and formed the styryl anhydro base (IV). When 4-hydroxynaphthaldehyde was used for this condensation, the reaction product was the anhydro base of benzohydroxystyryl, which did not form a salt with mineral acids.

The hydroxystyryl anhydro bases obtained were intraionoid dyes, possessing solvatochromic properties. Their color deepened with an increase in the polarity of the solvent. Thus, for example, anhydro base (IV) had an absorption maximum at 466 mμ in benzene and at 534 mμ in alcohol. The anhydro bases obtained from 4-hydroxynaphthaldehyde had absorption maxima at 496 and 538 mμ, respectively.

EXPERIMENTAL

Ethylperchlorate of 4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.15 g of the ethylperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine, 0.1 g of p-dimethylaminobenzaldehyde and 1.5 ml of acetic anhydride was heated on a water bath for 20 minutes. The crystals of styryl precipitated were collected and washed with water, alcohol and ether. The yield of styryl perchlorate was 0.18 g (68%); the m.p. was 211° and the absorption maximum in alcohol at 520 mμ.

Found %: N 6.21, 6.26. $C_{21}H_{25}O_4N_2SCl$. Calculated %: N 6.41.

Bromophenylate of 4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 1.7 g of the bromophenylate of 4-methyldihydrobenzohepta-1,5-thiazine, 0.76 g of p-dimethylaminobenzaldehyde and 4 ml of acetic anhydride was heated on a water bath for seven minutes. The crystals were collected and washed with water and alcohol. The yield was 0.95 g (41%); the m.p. was 220-221° and the absorption maximum at 546 mμ.

Found %: N 5.90, 6.00. $C_{25}H_{25}N_2SBr$. Calculated %: N 6.02.

The iodophenylate of 4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine was obtained by the usual method from the styryl bromophenylate and potassium iodide and had m.p. 232°.

Found %: N 5.28; I 24.76. $C_{25}H_{25}N_2SI$. Calculated %: N 5.46; I 24.80.

Iodomethylate of 2-methyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.7 g of the methyl methosulfate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine, 0.32 g of p-dimethylaminobenzaldehyde and 3 ml of acetic anhydride was heated on a water bath for 30 minutes. The precipitated styryl crystals, which weighed 0.5 g (51%), were converted by the usual method into the iodomethylate of 2-methyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine, which had m.p. 230° and an absorption maximum in alcohol at 522 mμ.

Found %: N 5.85, 5.96. $C_{21}H_{25}N_2SI$. Calculated %: N 6.03.

Ethylperchlorate of 2-methyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. Heating a mixture of 0.33 g of the ethylperchlorate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine, 0.15 g of p-dimethylaminobenzaldehyde and 2 ml of acetic anhydride for 20 minutes on a water bath yielded 0.34 g (72%) of the styryl. The lustrous, green needles had m.p. 230° and an absorption maximum in alcohol at 520 mμ.

Found %: N 6.14; Cl 8.05. $C_{22}H_{27}O_4N_2SCl$. Calculated %: N 6.22; Cl 7.88.

Iodophenylate of 2-methyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 1 g of the bromophenylate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine, 0.44 g of p-dimethylaminobenzaldehyde and 3 ml of acetic anhydride was heated on a water bath for 20 minutes. The styryl crystals were collected and washed with alcohol and ether. The yield of styryl was 0.63 g (46%). For purification, the styryl was converted into the iodophenylate of 2-methyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine by the usual method. The recrystallized iodide (from alcohol) had m.p. 232° and an absorption maximum in alcohol at 545 mμ.

Found %: N 4.99; I 24.05. $C_{26}H_{27}N_2SI$. Calculated %: N 5.33; I 24.14.

Bromomethylate of 2,2-dimethyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.62 g of the bromomethylate of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine, 0.31 g of p-dimethylaminobenzaldehyde and 3 ml of acetic anhydride was heated on a water bath for one hour. The precipitated crystals were recrystallized from alcohol. The yield of dye was 0.5 g (56%), the m.p. 230° and the absorption maximum in alcohol at 522 mμ. The action of alcoholic potassium hydroxide on an alcohol solution of the styryl formed a yellow base, which had an absorption maximum at 400 mμ. Acidification of a solution of the base gave a styryl salt with an absorption maximum at 522 mμ.

Found %: Br 18.37. $C_{22}H_{27}N_2SBr$. Calculated %: Br 18.54.

Bromoethylate of 2,2-dimethyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 1 g of the bromoethylate of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine, 0.4 g of p-dimethylaminobenzaldehyde and 5 ml of acetic anhydride was heated on a water bath for 30 minutes. The yield of styryl recrystallized from alcohol was 0.77 g (51%), the m.p. 247° and the absorption maximum in alcohol at 523 mμ. The free base of the styryl had an absorption maximum at 403 mμ.

Found %: Br 17.78. $C_{23}H_{29}N_2SBr$. Calculated %: Br 17.97.

Bromophenylate of 2,2-dimethyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.5 g of the bromophenylate of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine, 0.21 g of p-dimethylaminobenzaldehyde and 3 ml of acetic anhydride was heated for 30 minutes at 50-60°. The crystals of styryl were collected and washed with alcohol and ether. The yield of dye was 0.57 g (93%), the m.p. 210° (from alcohol) and the absorption maximum in alcohol at 547 mμ. The styryl base, obtained as above, had an absorption maximum at 410 mμ.

Found %: Br 16.31. $C_{27}H_{29}N_2SBr$. Calculated %: Br 16.22.

Bromophenylate of 2,2-dimethyl-4-(p-hydroxystyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.36 g of the bromophenylate of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine, 0.11 g of p-hydroxybenzaldehyde and 2 ml of acetic anhydride was heated at 80° for ten minutes. The condensation product was precipitated with ether and washed with a large amount of acetone. The yield of hydroxystyryl was 0.16 g (35%), the m.p. 188° and the absorption maximum in alcohol at 454 mμ.

Found %: N 2.87, 2.97; Br 17.09. $C_{25}H_{24}ONSBr$. Calculated %: N 3.00; Br 17.17.

Anhydro base of 2,2-dimethyl-5-phenyl-4-(p-hydroxystyryl)-dihydrobenzohepta-1,5-thiazine. To a heated solution of 0.2 g of the bromophenylate of 2,2-dimethyl-4-(p-hydroxystyryl)-dihydrobenzohepta-1,5-thiazine in 5 ml of alcohol was added a few drops of ammonia and hot water until turbidity appeared. The crystals which separated were recrystallized from aqueous alcohol. The yield of the anhydro base was 0.15 g (89%) and the absorption maximum in alcohol at 534 mμ, in chloroform, at 531 mμ, in benzene, at 489 mμ and in hexane, at 466 mμ.

Found %: N 3.53, 3.67. $C_{25}H_{23}ONS$. Calculated %: N 3.62.

Anhydro base of 2,2-dimethyl-5-phenyl-4-(p-hydroxybenzostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.2 g of the bromophenylate of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine, 0.13 g of 4-hydroxynaphthaldehyde and 3 ml of acetic anhydride was heated at 60° for 30 minutes. The yield of the bromophenylate of the hydroxystyryl was 0.25 g (80%) and the m.p. 182°. When dissolved in alcohol, the salt was hydrolyzed with the formation of the anhydro base with m.p. 158°. The absorption maximum of the anhydro base in alcohol was at 538 mμ, in chloroform at 526 mμ and in benzene at 496 mμ.

Found %: N 3.24, 3.43; S 7.40, 7.54. $C_{29}H_{25}ONS$. Calculated %: N 3.21; S 7.54.

SUMMARY

It was shown that quaternary salts of dihydrobenzohepta-1,5-thiazine derivatives, containing a methyl group in position 4, readily condense with p-dimethylaminobenzaldehyde and p-hydroxybenzaldehyde with the formation of the corresponding styryls. The quaternary salts of p-hydroxystyryls are readily converted into anhydro bases, whose colors deepen in more polar solvents.

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CYANINE DYES FROM SEVEN-MEMBERED HETEROCYCLIC SYSTEMS

II. SYNTHESIS OF STYRYL BASES AND THEIR ANALOGS IN THE DIHYDROBENZOHEPTA-1,5-THIAZINE SERIES

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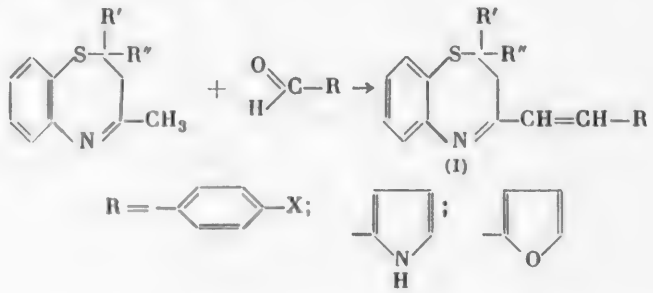
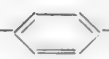
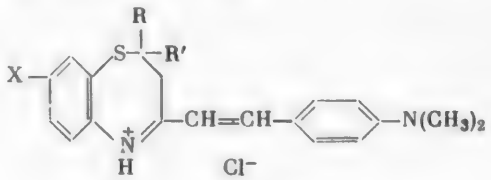
Kiev State University

2,2,4-Trimethyldihydrobenzohepta-1,5-thiazine and its closest homologs, which we prepared previously [1], possess an active methyl group in position 4 and readily condense with aromatic and heterocyclic aldehydes with the formation of styryl bases and their analogs.



(I)

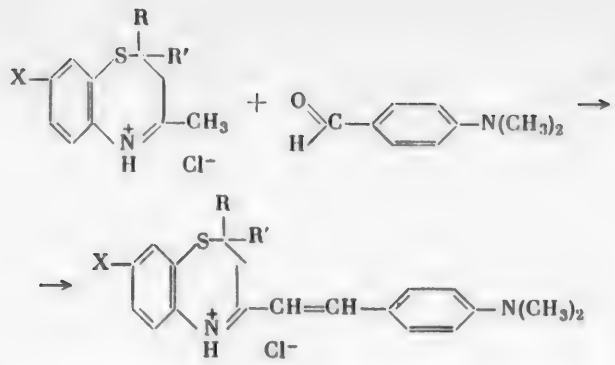
p-Dimethylaminostyryls (I, R =  $N(CH_3)_2$) were obtained by the fusion of equimolecular amounts of the free bases of 2,4-dimethyl- and 2,2,4-trimethyldihydrobenzohepta-1,5-thiazines and also their 8-nitro and 8-acetamino derivatives with p-dimethylaminobenzaldehyde on a water bath. The yellow styryl bases thus obtained reacted with mineral acids to form styryl dyes (II), which had a deeper color than the bases and the absorption maximum was shifted by 120 mμ.



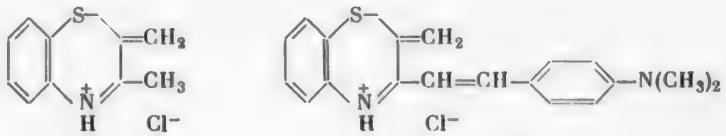
(II)

The same styryl dyes may be obtained directly from the appropriate hydrohalides of the seven-membered heterocyclic bases and p-dimethylaminobenzaldehyde in an acetic anhydride medium. The second method is preferable since the salts can be isolated from the reaction mixture more readily.

The styryls obtained in this way are unusual cyanine dyes containing hydrogen atoms instead of hydrocarbon radicals at the ring nitrogen atoms of the seven-membered ring. These dyes are readily decolorized by ammonia with the formation of styryl bases. They again give dyes with acids.



The condensation of o-aminothiophenol with 2'-chloro-2-methylbuten-1-one-3 gave the hydrochloride of 4-methyl-3-methylenedihydrobenzohepta-1,5-thiazine (III), which also reacted with p-dimethylaminobenzaldehyde to form a dye (IV).



(III) (IV)

The styryl (IV) had the same color as the styryl (Table 1, No. 2) obtained from the hydrochloride of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine. Their absorption maxima in ethanol solution lay at 523 and 520 mμ, respectively. This indicates that the formation of styryls involves the methyl group in position 4 both for the free bases and for the hydrohalides of heptathiazine bases. The methyl group in position 3 is not reactive.

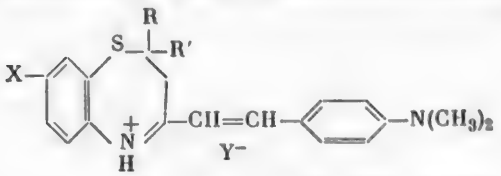
Table 1 shows data on the effect of some substituents on the color of p-dimethylaminostyryls and also their melting points and yields.

As the data presented (Table 1) and also that published previously [2] show, replacement of the alkyls by hydrogen atoms at the ring nitrogen atoms of the seven-membered rings does not affect the color of the styryls. The introduction of a nitro group into position 8 produces a bathochromic shift in the absorption maximum both in the free base and its salt by 35-38 mμ. An acetylamino group in position 8 produces a shift of the maximum toward longer wavelengths of the spectrum by 10 mμ.

The condensation of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine and its hydrochloride with benzaldehyde,

TABLE 1

Dependence of Color of p-Dimethylaminostyryls

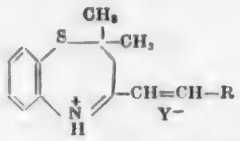


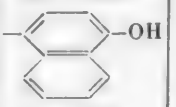
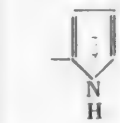
on the Nature of the Substituents

Sample No.	X	R	R'	Y⁻	λ_{max} (in mμ)		M.p.	Yield (%)
					salt	base		
1	H	H	CH_3	Cl	520	400	243°	70
2	H	CH_3	CH_3	Cl	520	400	256	66
3	NO_2	H	CH_3	ClO_4	555	436	216	55
4	NO_2	CH_3	CH_3	Br	555	436	234	74
5	CH_3CONH	CH_3	CH_3	Cl	530	—	256	52

TABLE 2

Change in the Color of Styryls and Their Analogs in Relation to the Composition and the Nature of the Radical R



Sample No.	R	Y⁻	λ_{max} (in mμ)		M.p.	Yield (%)
			salt	base		
1	C_6H_5	Cl	350	—	195°	80
2	p-$CH_3C_6H_4$	Cl	375	—	187	70
3	p-$NO_2C_6H_4$	Cl	355	—	183*	60
4	o-$NO_2C_6H_4$	Cl	355	—	121*	89
5	m-$NO_2C_6H_4$	ClO_4	355	—	202	64
6	p-OHC_6H_4	Cl	431	325	242	56
7	o-OHC_6H_4	Cl	422	—	164	19
8		Cl	495	385	232	35
9		Cl	407	338	225	66
10		ClO_4	455	375	221	61

*Melting point of base.

its nitro and hydroxy derivatives and also with furfural and α-pyrrolaldehyde proceeds similarly. The styryls and their analogs thus obtained have higher colors than the corresponding p-dimethylaminostyryls. This case is illustrated by Table 2. The same table gives the melting points and yields of the styryls.

Data presented in Tables 1 and 2 show that halochromism, i.e., a deepening in color on salt formation, is observed both in unsubstituted styryls and in nitro, hydroxy and dimethylamino derivatives. The shift in the absorption maximum toward the long-wave region of the spectrum on salt formation varies; for p-dimethylaminostyryls it is 120 mμ, for p-hydroxystyryls, 106-110 mμ and for nitrostyryls and also unsubstituted styryls the halochromic effect is insignificant. For the furan and pyrrole analogs of styryl, the bathochromic shift in the absorption maximum during salt formation is 69-80 mμ (Nos. 9 and 10, Table 2); here, as might be expected, the pyrrole analog has a deeper color than the furan one by 48 mμ.

EXPERIMENTAL

Hydrochloride of 2-methyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.5 g of 2,4-dimethyldihydrobenzohepta-1,5-thiazine hydrochloride, 0.4 g of p-dimethylaminobenzaldehyde and 2 ml of acetic anhydride was heated on a water bath for 30 minutes. The crystals of styryl were filtered off and washed with water, alcohol and ether. The yield of styryl hydrochloride was 0.2 g (25%), the m.p. 243° and the absorption maximum in alcohol at 520 mμ.

Found %: N 7.85, 7.88. $C_{20}H_{23}N_2SCl$. Calculated %: N 7.81.

A better yield of styryl was obtained by condensation of 2,4-dimethyldihydrobenzohepta-1,5-thiazine picrate with p-dimethylaminobenzaldehyde under analogous conditions. From 0.5 g of 2,4-dimethyldihydrobenzohepta-1,5-thiazine picrate and 0.2 g of p-dimethylaminobenzaldehyde, we obtained 0.5 g (70%) of styryl picrate with m.p. 198° (from alcohol) and the same absorption maximum (at 520 mμ).

Found %: N 12.80, 12.78. $C_{26}H_{25}O_7N_5S$. Calculated %: N 12.70.

2-Methyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. Ammonia was added dropwise to an alcohol solution of 0.36 g of 2-methyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine hydrochloride until a yellow color appeared. Then the warm solution of the base was diluted with water until turbidity appeared. The crystals of styryl base precipitated were recrystallized from alcohol. We obtained 0.2 g of free styryl base with m.p. 160° and an absorption maximum in alcohol at 400 mμ. With acids the styryl base formed a salt with a color 120 mμ deeper.

Found %: N 8.70, 8.74. $C_{20}H_{22}N_2S$. Calculated %: N 8.69.

Hydrochloride of 2,2-dimethyl-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 1 g of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine hydrochloride, 0.6 g of p-dimethylaminobenzaldehyde and 5 ml of acetic anhydride was heated on a water bath for ten minutes. The crystals of styryl were filtered and washed with water, alcohol and ether. The yield of styryl was 0.98 g (66%), the m.p. 256° and the absorption maximum in alcohol at 520 mμ. The action of ammonia on an alcohol solution of the styryl salt gave the styryl base, which had an absorption maximum at 400 mμ.

Found %: N 7.47, 7.57. $C_{21}H_{25}N_2SCl$. Calculated %: N 7.52.

Fusion of the free base of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine with p-dimethylaminobenzaldehyde on a water bath (without solvent) and subsequent treatment of an alcohol solution with hydrochloric acid yielded a styryl hydrochloride, identical with that described above, in 60% yield.

Perchlorate of 2-methyl-8-nitro-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.3 g of 2,4-dimethyl-8-nitrodihydrobenzohepta-1,5-thiazine hydrobromide, 0.15 g of p-dimethylaminobenzaldehyde and 1.5 ml of acetic anhydride was heated on a water bath for ten minutes. The crystals of styryl hydrobromide were dissolved in alcohol and a few drops of perchloric acid added. The precipitated crystals of styryl perchlorate were recrystallized from alcohol. The yield of styryl was 0.25 g (55%), the m.p. 216° and the absorption maximum in alcohol at 555 mμ.

Found %: N 9.00, 9.02. $C_{20}H_{22}O_6N_3SCl$. Calculated %: N 8.98.

2-Methyl-8-nitro-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. Ammonia was added to an alcohol solution of 2-methyl-8-nitro-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine perchlorate until the red-violet color of the solution disappeared. The precipitated styryl base was recrystallized from alcohol. We obtained orange needles of styryl base with m.p. 177° and an absorption maximum in alcohol at 436 mμ.

Found %: N 11.50, 11.51. $C_{20}H_{21}O_2N_3S$. Calculated %: N 11.44.

Hydrobromide of 2,2-dimethyl-8-nitro-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.68 g of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine hydrobromide, 0.35 g of p-dimethylaminobenzaldehyde and 7 ml of acetic anhydride was heated on a water bath for 20 minutes. The precipitated styryl crystals were recrystallized from alcohol. The yield was 0.7 g (74%), the m.p. 234° and the absorption maximum in alcohol at 555 mμ. The action of ammonia on an alcohol solution of the styryl salt yielded the styryl base with an absorption maximum at 438 mμ.

Hydrochloride of 2,2-dimethyl-8-acetylamino-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. An ether solution of 0.3 g of 2,2,4-trimethyl-8-aminodihydrobenzohepta-1,5-thiazine was saturated with dry hydrogen chloride. The amine hydrochloride obtained was dissolved in 7 ml of acetic anhydride, 0.25 g of p-dimethylaminobenzaldehyde added and the mixture heated on a water bath for 30 minutes. The violet crystals of styryl precipitated were collected and washed well with water and alcohol. The yield of styryl hydrochloride was 0.26 g (52%) and the absorption maximum in alcohol at 530 mμ.

Found %: N 9.64, 9.51. $C_{23}H_{28}N_3SCl$. Calculated %: N 9.78.

Hydrochloride of 3-methylene-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine. We prepared

the starting heptathiazine base, 4-methyl-3-methylenedihydrobenzohepta-1,5-thiazine, in the form of the hydrochloride by condensation of 2[1]-chloro-2-methylbuten-1-one-3 with o-aminothiophenol at room conditions in benzene solution [3]. A mixture of 2.25 g of 4-methyl-3-methylenedihydrobenzohepta-1,5-thiazine hydrochloride, 0.49 g of p-dimethylaminobenzaldehyde and 4 ml of acetic anhydride was kept at room temperature for 5-6 hours. The precipitated crystals of styryl hydrochloride (1.95 g; 54%) were dissolved in an alcohol solution of ammonia. The free styryl base formed was filtered and several drops of concentrated hydrochloric acid added to the filtrate until an intense red-violet color appeared. The precipitated crystals of styryl hydrochloride were collected and washed with water and alcohol. The hydrochloride of 3-methylene-4-(p-dimethylaminostyryl)-dihydrobenzohepta-1,5-thiazine, purified in this way, had m.p. 227° and an absorption maximum in alcohol at 522 mμ. The styryl base had an absorption maximum at 405 mμ.

Found %: N 7.51, 7.79. $C_{20}H_{21}N_2SCl$. Calculated %: N 7.86.

Another method of purifying the styryl consisted of chromatographing an alcohol solution on an aluminum oxide column. A solution of styryl base was obtained in this way and was converted into the hydrochloride by the addition of hydrochloric acid.

Hydrochloride of 2,2-dimethyl-4-styryldihydrobenzohepta-1,5-thiazine. A mixture of 0.5 g of 2,2,4-trimethylhydrobenzohepta-1,5-thiazine hydrochloride and 0.5 g of benzaldehyde was heated on a water bath for ten minutes. The salt first dissolved in the benzaldehyde, but toward the end of the heating, the contents of the tube crystallized. The crystals were collected and washed with alcohol and ether. The yield of styryl was 0.64 g (88%), the m.p. 195° (from alcohol) and the absorption maximum at 350 mμ.

Found %: N 4.16, 4.04. $C_{19}H_{20}NSCl$. Calculated %: N 4.34.

2,2-Dimethyl-4-styryldihydrobenzohepta-1,5-thiazine. To a heated solution of 0.1 g of 2,2-dimethyl-4-styryldihydrobenzohepta-1,5-thiazine hydrochloride in 2 ml of alcohol were added several drops of ammonia and then water to the appearance of turbidity. The precipitated crystals of styryl base (0.5 g) had m.p. 75°.

Found %: N 4.70, 4.56. $C_{19}H_{19}NS$. Calculated %: N 4.76.

Hydrochloride of 2,2-dimethyl-4-(p-methylstyryl)-dihydrobenzohepta-1,5-thiazine. This styryl was prepared similarly to the previous one. From 1.2 g of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine hydrochloride and 2 g of p-tolualdehyde we obtained 1.6 g (70%) of styryl hydrochloride with m.p. 187° (from alcohol) and an absorption maximum at 375 mμ.

Found %: Cl 10.17; N 4.31. $C_{20}H_{22}NSCl$. Calculated %: Cl 10.32; N 4.08.

2,2-Dimethyl-4-(p-methylstyryl)-dihydrobenzohepta-1,5-thiazine was isolated from an alcohol solution of the styryl hydrochloride by the action of ammonia; the light-yellow crystals had m.p. 131°.

Found %: N 4.72. $C_{20}H_{21}NS$. Calculated %: N 4.56.

The methyl group in the para position did not possess active hydrogen atoms.

2,2-Dimethyl-4-(p-nitrostyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 1 g of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine and 0.74 g of p-nitrobenzaldehyde was fused on a water bath for ten minutes. At the end of the heating the mixture crystallized. After recrystallization from alcohol, the preparation had m.p. 183° and the yield was 1 g (60%). The nitrostyryl base obtained reacted with hydrochloric acid to form a hydrochloride with an absorption maximum at 355 mμ.

Found %: N 7.78, 7.80. $C_{19}H_{18}O_2N_2S$. Calculated %: N 7.93.

2,2-Dimethyl-4-(o-nitrostyryl)-dihydrobenzohepta-1,5-thiazine. This product was obtained by fusion of 1 g of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine with 0.74 g of o-nitrobenzaldehyde as in the previous experiment. The yield of o-nitrostyryl after recrystallization from alcohol was 1.4 g (89%) and the m.p. 121°. 2,2-Dimethyl-4-(o-nitrostyryl)-dihydrobenzohepta-1,5-thiazine hydrochloride had an absorption maximum in alcohol at 355 mμ.

Found %: N 7.75, 7.78. $C_{19}H_{18}O_2N_2S$. Calculated %: N 7.93.

The third isomer, 2,2-dimethyl-4-(m-nitrostyryl)-dihydrobenzohepta-1,5-thiazine was obtained similarly to the previous two by fusion of the starting components on a water bath. It was isolated in the form of its per-

chlorate by the addition of perchloric acid to an alcohol solution of the m-nitrostyryl base. The yield was 64% and the perchlorate had m.p. 202° and an absorption maximum at 355 mμ. The base, 2,2-dimethyl-4-(m-nitrostyryl)-dihydrobenzohepta-1,5-thiazine, was isolated from the perchlorate in the usual way and had m.p. 157°.

Found %: N 7.62, 7.78. $C_{19}H_{18}O_2N_2S$. Calculated %: 7.93.

Hydrochloride of 2,2-dimethyl-4-(p-hydroxystyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.5 g of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine hydrochloride, 0.3 g of p-hydroxybenzaldehyde and 3 ml of acetic anhydride was heated on a water bath for five minutes. The precipitated crystals of hydrochloride were recrystallized from alcohol. The yield was 0.38 g (56%), the m.p. 242° and the absorption maximum in alcohol at 431 mμ.

Found %: N 4.10; Cl 10.13. $C_{19}H_{20}ONSCl$. Calculated %: N 4.05; Cl 10.29.

2,2-Dimethyl-4-(p-hydroxystyryl)-dihydrobenzohepta-1,5-thiazine. 0.1 g of the p-hydroxystyryl hydrochloride was mixed with 5 ml of alcohol and the mixture heated to boiling. To the heated suspension was added several drops of ammonia and the precipitate dissolved. Water was added to the solution until turbidity appeared. Crystals of free styryl base separated in the form of light-yellow scales (0.07 g) and had m.p. 202° and an absorption maximum in alcohol at 325 mμ.

Found %: N 4.51, 4.29. $C_{19}H_{19}ONS$. Calculated %: N 4.53.

Hydrochloride of 2,2-dimethyl-4-(o-hydroxystyryl)-dihydrobenzohepta-1,5-thiazine. A mixture of 0.5 g of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine hydrochloride, 0.3 g of salicylaldehyde and 5 ml of acetic anhydride was heated on a water bath for one hour. The crystals of o-styryl hydrochloride were recrystallized from alcohol. The yield was 0.14 g (19%), the m.p. 164° and the absorption maximum in alcohol at 422 mμ. The action of ammonia on the hydroxystyryl hydrochloride liberated the free base of 2,2-dimethyl-4-(o-hydroxystyryl)-dihydrobenzohepta-1,5-thiazine as light-yellow crystals with m.p. 155°.

Found %: N 4.74, 4.71. $C_{19}H_{19}ONS$. Calculated %: N 4.53.

Hydrochloride of 2,2-dimethyl-4-(p-hydroxy-2',3'-benzostyryl)] dihydrobenzohepta-1,5-thiazine was obtained analogously. From 0.5 g of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine hydrochloride and 0.2 g of 4-hydroxynaphthaldehyde we obtained 0.29 g (35%) of hydroxystyryl hydrochloride. After recrystallization from alcohol, the hydroxystyryl hydrochloride had m.p. 232° and an absorption maximum at 459 mμ.

Found %: N 3.75, 3.67. $C_{23}H_{22}ONSCl$. Calculated %: N 3.54.

The free base, 2,2-dimethyl-4-hydroxy-2',3'-benzostyryl)-dihydrobenzohepta-1,5-thiazine, obtained by the usual method, had m.p. 196° and an absorption maximum in alcohol at 385 mμ.

Found %: N 3.80, 4.02. $C_{23}H_{21}ONS$. Calculated %: N 3.89.

Hydrochloride of 2,2-dimethyl-4-[β-(α-furyl)-ethenyl]-dihydrobenzohepta-1,5-thiazine. A mixture of 2.4 g of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine and 6 g of furfural was heated on a water bath for 15 minutes. Then 6 ml of alcohol and hydrochloric acid were added to the reaction product. The hydrochloride of the reaction product thus obtained crystallized. The yield of it was 2.8 g (67%). After recrystallization from alcohol, the preparation (yellow needles) had m.p. 225° and an absorption maximum in alcohol at 407 mμ.

Found %: N 4.25, 4.30. $C_{17}H_{18}ONSCl$. Calculated %: N 4.15.

2,2-Dimethyl-4-[β-(α-furyl)-ethenyl]-dihydrobenzohepta-1,5-thiazine was isolated from an alcohol solution of its hydrochloride by means of ammonia. The light-yellow crystals had m.p. 136° and an absorption maximum at 338 mμ.

Found %: N 4.52. $C_{17}H_{17}ONS$. Calculated %: N 4.62.

Perchlorate of 2,2-die ethyl-4-[β-(α-pyrryl)-ethenyl]-dihydrobenzohepta-1,5-thiazine. This styryl analog was obtained analogously to the furan analog. From 1 g of 2,2,4-trimethyldihydrobenzohepta-1,5-thiazine and 0.5 g of α-pyrrolaldehyde we obtained 0.9 g of 2,2-dimethyl-4-[β-(α-pyrryl)-ethenyl]-dihydrobenzohepta-1,5-thiazine perchlorate with m.p. 221° and an absorption maximum in alcohol at 455 mμ. The action of ammonia on an alcohol solution of the perchlorate yielded the free base with an absorption maximum in alcohol at 375 mμ.

Found %: N 7.24, 7.30. $C_{17}H_{19}O_4N_2SCl$. Calculated %: N 7.31.

SUMMARY

1. It was shown that a methyl group in position 4 of free bases and hydrohalides of benzohepta-1,5-thiazines was active and readily condensed with aromatic and heterocyclic aldehydes to form styryls and their analogs.

2. The salts of dimethylaminostyryls obtained in the dihydrobenzohepta-1,5-thiazine series had deeper colors than the bases by 120 mμ. Deepening in color on salt formation was also observed with hydroxystyryls (106-110 mμ) and also with furan and pyrrole analogs of styryls in the dihydrobenzohepta-1,5-thiazine series (69-80 mμ).

3. It was established that nitro and acetylamino groups in position 8 deepened the color of dimethylaminostyryls by 35 and 10 mμ, respectively.

4. Replacement of the alkyls of dimethylaminostyryls of the dihydrobenzohepta-1,5-thiazine series by hydrogen atoms at the ring nitrogen atoms (position 5) did not affect the color of the styryls.

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THE ALKALOIDS OF AMMOTHAMNUS SONGORICUS

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Ammothamnus songoricus (Leguminosae family) is a ramose shrub growing in Central Asia. P.S. Massagetov established that the plant contained alkaloids. He also provided the material used in this investigation, which was collected in June (before the fruit had ripened) in the middle section of the River Ili.

The whole of the plant above ground was extracted. The total alkaloids of this plant (about 1%) were separated into two fractions by extraction with ether and chloroform. The ether extracted consisted almost completely of sophocarpine. The chloroform fraction yielded an optically active ($[\alpha]_D$ +21.6°) alkaloid with m.p. 198-200°, crystallizing with one molecule of water, which it lost on drying but readily absorbed again in air. The elementary analysis of this base corresponded to the composition of $C_{15}H_{24}O_2N_2 \cdot H_2O$. It did not contain a methylimide group. The only crystalline salts that could be obtained were the perchlorate with m.p. 219-220° (with decomp.) and the picrate with m.p. 215° (with decomp.); a methiodide with m.p. 285° (with decomp.) was also obtained.

From the empirical formula of the alkaloid and also its properties it was conjectured that the alkaloid we isolated was the N-oxide of matrine. Actually, on reducing the base with zinc dust (in acid solution) we obtained matrine. According to the description of Kondo et al., the N-oxide of matrine exists in two hydrate forms, one of which melts at 208° and has $[\alpha]_D$ +29.7°, and the second at 77-80° [1]. In a later communication, Ochiai corrected the data of the first article and also described two forms of the N-oxide of matrine: one with m.p. 208° (anhydrous form) and the other with m.p. 161-163°, $[\alpha]_D$ +47.7° (hydrated form) [2].

By chromatographic fractionation of the chloroform fraction obtained from the plant on Al_2O_3, we isolated a series of fractions with various melting points from 153 to 207° and specific rotations from +20 to +26°. In its properties, the base with m.p. 207° corresponded to matrine N-oxide described in the work of Ochiai [2] During prolonged storage, the melting point of this substance fell to 198-200°.

As regards the other fractions with lower melting points, all these bases had very similar specific rotations all contained water of crystallization and all gave good yields of matrine when reduced with zinc dust in an acid medium.

If the base with m.p. 198-200°, isolated from the plant, was recrystallized from aqueous acetone, then in agreement with the first work of the Japanese authors [1], we obtained crystals with m.p. 77-80°; however, as the material stood in air, the solvent of crystallization disappeared and the melting point of the material gradually rose.

For direct comparison of our alkaloid with matrine N-oxide, we oxidized matrine with hydrogen peroxide. The matrine N-oxide formed was similar to the base we isolated from the plant and was obtained in different forms with melting points from 153 to 188°, which did not depress the melting points of corresponding fractions.

Thus, the results we obtained confirmed the identity of the alkaloid we isolated and matrine N-oxide.

Despite certain differences both in constants and in formula (as is shown by the table below), the base we isolated from Ammothamnus songoricus is apparently identical with the alkaloid ammothamnine, obtained by Sadykov and Lazur'evskii from Ammothamnus lehmanni Bge. [3].

Alkaloid	Formula	Melting point		$[\alpha]_D$
		base	picrate	
Ammothamnine from Ammothamnus lehmanni Bge.	$C_{15}H_{24}O_3N_2$ or $C_{14}H_{20}O_2N(OH)\cdot(NCH_3)$	199-201°	212-214° (decomp.)	Optically inactive
Base from Ammothamnus songoricus	$C_{15}H_{24}O_2N_2\cdot H_2O$	198-200	215 (decomp.)	+21.6°

EXPERIMENTAL

Extraction of alkaloids from plant. Ground plant (2.5 kg) was extracted with isopropyl alcohol. The residue from the alcohol extract, after evaporation of the alcohol in vacuum, was dissolved in 10% sulfuric acid. The acid solution was washed with chloroform (to remove tarry materials in it), made alkaline with ammonia and the bases extracted with ether (extract A) and then with chloroform (extract B).

Treatment of ether extract A. Isolation of sonhocarpine. The residue after evaporation of the ether was converted into a hydroiodide (9 g) with m.p. 290°. The base isolated from the hydroiodide had m.p. 80-81° and $[\alpha]_D$ −29.3°, and did not depress the melting point of sophocarpine.

Treatment of chloroform extract B. Isolation of matrine N-oxide. The alkaloid obtained after evaporation of the chloroform was treated with acetone. A base which was difficultly soluble in acetone precipitated (19.3 g) and had m.p. 198-200° and $[\alpha]_D$ +21.6° (c 65, alcohol).

Found %: C 64.15, 64.06; H 8.93, 9.13; N 10.10; H_2O 6.43. $C_{15}H_{24}O_2N_2\cdot H_2O$. Calculated %: C 63.83; H 9.22; N 9.92; H_2O 6.43.

The picrate was formed by mixing alcohol solutions of the base and picric acid. The m.p. was 215° (with decomp.) (from a mixture of alcohol and water).

The perchlorate was obtained from the hydrochloride in an aqueous solution. The m.p. was 219-220° (with decomp.) (from water).

The methiodide was obtained by the action of CH_3I in methanol (boiling for two hours). The m.p. was 285° (with decomp.) (from methanol).

Reduction of matrine N-oxide. Preparation of matrine. 2 g of base with m.p. 198-200° in 40 ml of 10% H_2SO_4 was reduced with zinc dust (8 g) over a period of 24 hours. The filtered solution was made alkaline with NaOH and extracted with ether. We obtained 1.3 g of matrine with m.p. 73-75° and $[\alpha]_D$ +37.5° (c 4.8, $CHCl_3$). It did not depress the melting point of a sample of α-matrine obtained previously.

Catalytic hydrogenation (with Raney nickel catalyst) of the base with m.p. 198-200° also yielded matrine melting at 74-76°; two moles of hydrogen were consumed.

Fractionation of total alkaloids (B) by chromatography on Al_2O_3. A solution of 12 g of base (B) in 50 ml of $CHCl_3$ was passed through 500 g of Al_2O_3. Elution with chloroform yielded 12 fractions. All the fractions, apart from the first two, yielded crystalline substances with gradually increasing melting points from 153-200°; the specific rotations of the fractions varied over the range from +26° to +20°; the R_f varied from 0.25 to 0.3.*

When the middle fractions (with m.p. 182-184° and 185-187°) were boiled with acetone we obtained a substance with m.p. 207-207.5°, which was difficultly soluble in acetone, and the solution deposited a base with m.p. 153-155°. The picrates obtained from these two substances had m.p. 215° (with decomp.) (according to literature data, m.p. 215°).

Reduction of base with m.p. 153-155°. Preparation of matrine. 0.3 g of base with m.p. 153-155° (obtained from the chloroform extract B) in an alcohol solution was shaken in an atmosphere of hydrogen with 1 g of Raney

*Chromatography on No. 4 paper was used for qualitative characterization of the fractions obtained (solvent — upper phase of a mixture of isoamyl alcohol—water—acetic acid in the ratio 50:50:1, time six hours, temperature 18-19°, and developer, a modified Dragendorff reagent).

nickel catalyst (paste). Two moles of hydrogen were absorbed in the reduction; the alcohol was removed in vacuum. We obtained matrine (0.24 g) with m.p. 74-76° and $[\alpha]_D$ +39° (c 1.2, alcohol).

Oxidation of matrine with hydrogen peroxide. Preparation of matrine N-oxide. 10 g of matrine with m.p. 75-77° was oxidized with 3% hydrogen peroxide (100 ml) for two days at 20°. The solution was washed with ether (to remove unreacted matrine), made alkaline with ammonia, and the matrine N-oxide formed extracted with chloroform. The chloroform was removed and the residue (6 g) treated with acetone to give substances with different melting points from 153-155° (I) to 186-188° (II), depending on the treatment conditions.• Mixed melting points of substances (I) and (II) with bases, isolated by chromatography of the total alkaloids (B) and having corresponding melting points, were not depressed.

SUMMARY

1. The previously known base sophocarpine and an alkaloid of the composition $C_{15}H_{24}O_2N_2 \cdot H_2O$ were isolated from Ammothamnus songoricus.

2. It was established that the alkaloid isolated was matrine N-oxide.

LITERATURE CITED

[1] H. Kondo, E. Ochiai and K. Tsuda, Arch. Pharm. 275, 493 (1937).

[2] E. Ochiai, Ber. 71, 939 (1938).

[3] A.S. Sadykov and G.V. Lazur'evskii, J. Gen. Chem. 13, 314 (1943).

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•Several melting points are also given in the work of Ochiai [2] for matrine N-oxide.

SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET CHEMICAL LITERATURE

Abbreviation (Transliterated)	Significance
FIAN	Phys. Inst. Acad. Sci. USSR
GIPKh	State Institute of Applied Chemistry
GIREDMET	State Rare Metals Scientific Research Institute
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GLAVKhIM	Main Administration of the Chemical Industry
GOI	State Optical Institute
GONTI	State United Sci.-Tech. Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
Gostoptekhizdat	State Scientific and Technical Publishing house of the Petroleum and Mineral Fuel Industry
GTTI	State Tech. and Theor. Lit. Press
IFKhA	Institute of Physicochemical Analysis
IL	Foreign Lit. Press
IOKhAN	Institute of Organic Chemistry of the Academy of Sciences of the USSR
IONKh	Institute of General and Inorganic Chemistry (N. S. Kurnakov)
IONKhAN	Institute of General and Inorganic Chemistry of the Academy of Sciences of the USSR
INBI	Institute of Biochemistry
IREA	Institute of Chemical Reagents
ISN (Izd. Sov. Nauk)	Soviet Science Press
IVKhTI	Ivanovo Chemical Engineering Institute
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
KEIN	Colloid Electrochemical Institute
Khimizdat	Chemistry Press
LGU	Leningrad State University
LIM	Leningrad Institute of Metals
Metallurgizdat	Metallurgy Press
MITKhT	Moscow Institute of Fine Chemical Technology
OIYaI	Joint Institute of Nuclear Studies
OKhN	Division of Chemical Science
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Division of Technical Science
RIAN	Radium Institute, Academy of Sciences of the USSR
RZhKhim	Chemical Abstract Journal (USSR)
VKhO	All-Union Chemical Society (Mendeleev)
ZhFKh	Journal of Physical Chemistry (USSR)
ZhRKhO	Journal of the Russian Chemical Society

Note: Abbreviations not on this list and not explained in the translation have been transliterated no further information about their significance being available to us. — Publisher.

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